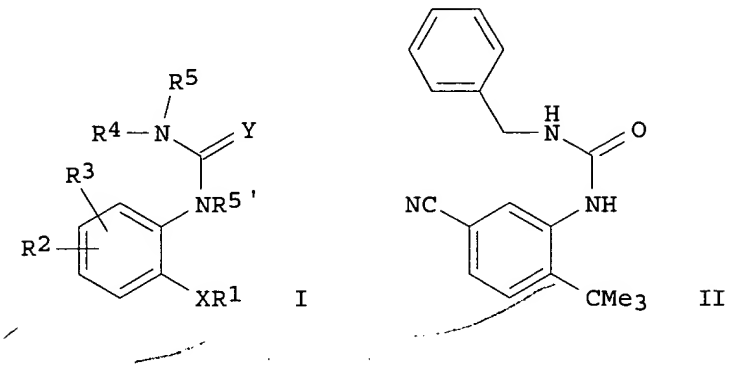
4 ANSWER 22 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI



I II

AB Title compds. I [X = single bond, O, CO, S, NH, or alkylimino; Y = O, S, or NCN; R1 = alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl; R2 = H, alkyl, haloalkyl, alkenyl, alkynyl, cyano, NO2, CHO, CO2H, halo, (un)substituted amino, etc.; R3 = H, alkyl, OH, alkoxy, (un)substituted amino, cyano, NO2; R4 = aryl, aralkyl, heterocyclo, heterocycloalkyl; R5, R5' = H, alkyl, (un)substituted alkylamino, haloalkyl; or R4R5 form ring with 5 to 7 members and optional O, S, or (un)substituted NH] and salts are claimed, along with 18 specific compds. which were also prepd. These compds. have potassium channel activating activity and are useful, e.g., as cardiovascular agents (no data). For example, tert-butylbenzene underwent 2,4-dinitration (70%), redn. of the 4-nitro group to amino (86%), diazotization and cyanation of the group to give a benzonitrile (42%), and redn. of the remaining nitro group with SnCl2 (100%) to give 3-amino-4-(tert-butyl)benzonitrile. Reaction of this with benzyl isocyanate gave title compd. II in 70% yield.

AN 1995:733459 CAPLUS
DN 123:143653
TI Biaryl ureas and related compounds for use as cardiovascular agents.
IN Atwal, Karnail; Ferrara, Francis N.; Ding, Charles Z.
PA USA
SO Can. Pat. Appl., 39 pp.
CODEN: CPXXEB
DT Patent
LA English
FAN.CNT 1

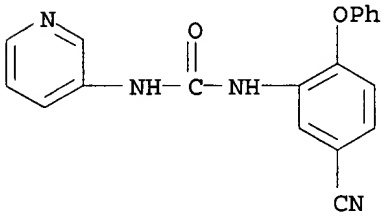
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CA 2132771	AA	19950408	CA 1994-2132771	19940923
	US 5547966	A	19960820	US 1993-134195	19931007
	EP 656350	A1	19950607	EP 1994-306813	19940916
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	AU 9474463	A1	19950427	AU 1994-74463	19941006
	AU 690133	B2	19980423		
	JP 07188151	A2	19950725	JP 1994-243895	19941007
PRAI	US 1993-134195		19931007		

OS MARPAT 123:143653
IT **166263-16-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biaryl ureas and analogs as cardiovascular agents)

RN 166263-16-7 CAPLUS

CN Urea, N-(5-cyano-2-phenoxyphenyl)-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



L4 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

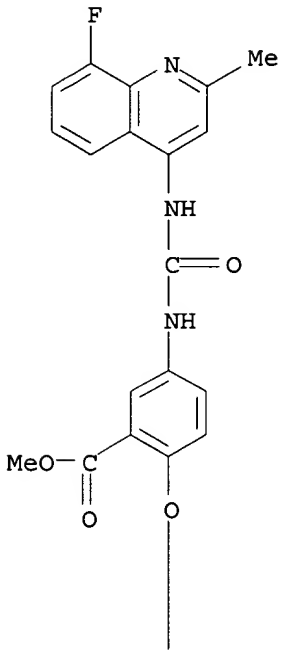
AB The title compds. [I; Z = O, S; R1 = alkyl, alkenyl, alkoxy, etc.; R2-R6 = alkyl, alkenyl, alkoxy, etc.; adjacent pair of R2-R6 together with the carbon atoms to which they are attached form (un)substituted carbocyclyl, heterocyclyl; R7 = alkyl, alkenyl, alkoxy, etc.; n = 0-3] and their pharmaceutically acceptable salts which are non-peptide antagonists of human orexin receptors, in particular orexin-1 receptors, were prepd. E.g., treatment of 4-amino-2-methylquinoline with carbonyl diimidazole in CH2Cl2 followed by addn. of 6-amino-2-methylbenzoxazole afforded II which showed pKb > 6.0 against orexin-1 receptor. In particular, compds. I are of potential use in the treatment of obesity including obesity obsd. in Type 2(non-insulin-dependent) diabetes patients and/or sleep disorders.

AN 2000:573791 CAPLUS
DN 133:164009
TI Preparation of phenyl ureas and thioureas as orexin receptor antagonists
IN Coulton, Steven; Johns, Amanda; Porter, Roderick Alan
PA Smithkline Beecham Plc, UK
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

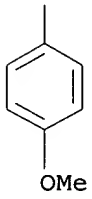
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000047577	A1	20000817	WO 2000-EP1150	20000210
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1150977	A1	20011107	EP 2000-906324	20000210
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	GB 1999-3266	A	19990212		
	GB 1999-26430	A	19991108		
	WO 2000-EP1150	W	20000210		

OS MARPAT 133:164009
IT **288151-08-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of Ph ureas and thioureas as orexin receptor antagonists)
RN 288151-08-6 CAPLUS
CN Benzoic acid, 5-[[[(8-fluoro-2-methyl-4-quinolinyl)amino]carbonyl]amino]-2-(4-methoxyphenoxy)-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L2 71 S L1 FUL

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L3 8 S L2

FILE 'CAPLUS' ENTERED AT 16:37:54 ON 09 SEP 2002
L4 26 S L2
L5 0 S L4 NOT L3

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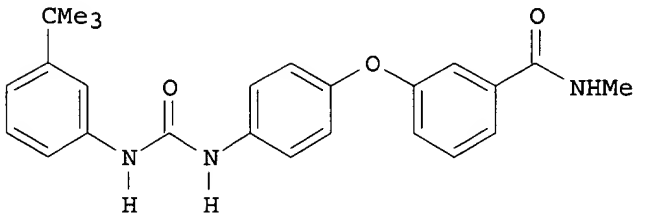
26 L2
L6 0 L4 NOT L3

=> d abs bib fhitstr l4 1-26

L4 ANSWER 1 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI



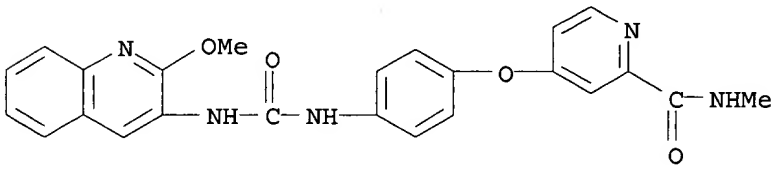
II

AB Title compds., e.g., RNHCONHZOR1 [I; R = C6H4(CMe3)-3, 2-methoxy-5-trifluoromethylphenyl, 4-chloro-3-trifluoromethylphenyl, 2-methoxy-3-quinolyl, etc.; R1 = (un)substituted acylphenyl, -acylpyridinyl, etc.; Z = (un)substituted 1,3- or -1,4-phenylene] were prepd. Thus, 4-(H2N)C6H4OC6H4(CONHMe)-4 (prepn. given) was condensed with 3-(Me3C)C6H4NH2 and CO(OCCl3)2 to give title compd. II. Data for biol. activity of title compds. were given.
AN 2002:615574 CAPLUS
TI Preparation of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors
IN Dumas, Jacques; Riedl, Bernd; Khire, Uday; Wood, Jill E.; Sibley, Robert N.; Monahan, Mary-Katherine; Renick, Joel; Gunn, David E.; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.
PA Bayer Corporation, USA
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002062763	A2	20020815	WO 2002-US203361	20020207

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,

US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2001-777920 A 20010207
IT **432050-22-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors)
RN 432050-22-1 CAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



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 NEWS  3  Apr 09  BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS  4  Apr 09  ZDB will be removed from STN
 NEWS  5  Apr 19  US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
 NEWS  6  Apr 22  Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
 NEWS  7  Apr 22  BIOSIS Gene Names now available in TOXCENTER
 NEWS  8  Apr 22  Federal Research in Progress (FEDRIP) now available
 NEWS  9  Jun 03  New e-mail delivery for search results now available
 NEWS 10  Jun 10  MEDLINE Reload
 NEWS 11  Jun 10  PCTFULL has been reloaded
 NEWS 12  Jul 02  FOREGE no longer contains STANDARDS file segment
 NEWS 13  Jul 22  USAN to be reloaded July 28, 2002;
                  saved answer sets no longer valid
 NEWS 14  Jul 29  Enhanced polymer searching in REGISTRY
 NEWS 15  Jul 30  NETFIRST to be removed from STN
 NEWS 16  Aug 08  CANCERLIT reload
 NEWS 17  Aug 08  PHARMAMarketLetter(PHARMAML) - new on STN
 NEWS 18  Aug 08  NTIS has been reloaded and enhanced
 NEWS 19  Aug 19  Aquatic Toxicity Information Retrieval (AQUIRE)
                  now available on STN
 NEWS 20  Aug 19  IFIPAT, IFICDB, and IFIUDB have been reloaded
 NEWS 21  Aug 19  The MEDLINE file segment of TOXCENTER has been reloaded
 NEWS 22  Aug 26  Sequence searching in REGISTRY enhanced
 NEWS 23  Sep 03  JAPIO has been reloaded and enhanced

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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DICTIONARY FILE UPDATES: 8 SEP 2002 HIGHEST RN 448182-31-8

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Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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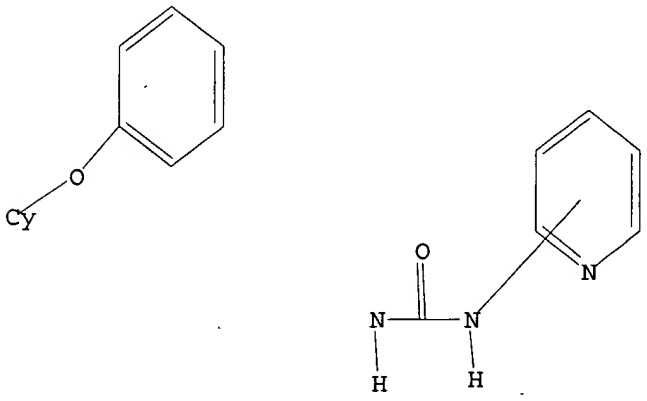

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SEARCH TIME: 00.00.06

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FILE 'USPATFULL' ENTERED AT 16:37:15 ON 09 SEP 2002
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

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CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

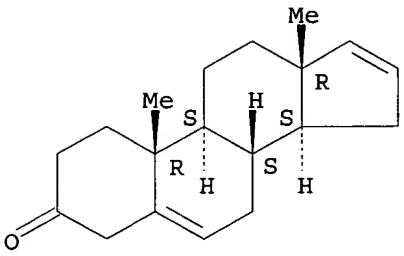
=> s l2
L3 8 L2

=> d abs bib hitstr 1-8

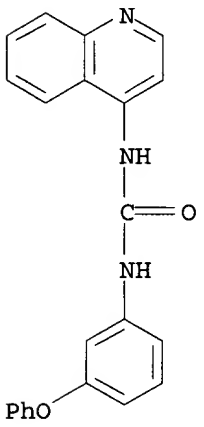
L3 ANSWER 1 OF 8 USPATFULL
AB Phenyl urea and phenylthiourea derivatives, processes for their production and their uses as pharmaceuticals are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:152635 USPATFULL
TI Phenyl urea and phenyl thiourea derivatives as HFGAN72 antagonists
IN Chan, George, Wynnewood, PA, United States
Johns, Amanda, Bishop's Stortford, UNITED KINGDOM
Jurewicz, Anthony, Royersford, PA, United States
Porter, Roderick Alan, Ashwell, UNITED KINGDOM
Widdowson, Katherine, King of Prussia, PA, United States
PA SmithKline Beecham p.l.c., Brentford, UNITED KINGDOM (non-U.S. corporation)
PI US 6410529 B1 20020625
WO 9909024 19990225
AI US 2000-485623 20000510 (9)
WO 1998-GB2437 19980813
20000510 PCT 371 date
PRAI GB 1997-17178 19970814
GB 1998-7756 19980408
DT Utility
FS GRANTED
EXNAM Primary Examiner: Davis, Zinna Northington
LREP Sieburth, Kathryn, McCarthy, Mary E., Kinzig, Charles M.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 2275
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **103614-70-6P**, Androsta-5,16-dien-3-one
(steroids as neurochem. stimulators of the VNO to alleviate pain)
RN 103614-70-6 USPATFULL
CN Androsta-5,16-dien-3-one (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **220844-29-1P**
(prepn. of quinolinylureas and related compds. as HFGAN72 antagonists)
RN 220844-29-1 USPATFULL
CN Urea, N-(3-phenoxyphenyl)-N'-4-quinolinyl-, monohydrochloride (9CI) (CA INDEX NAME)

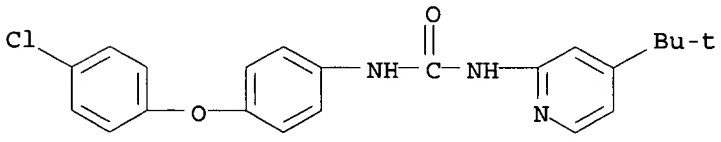


● HCl

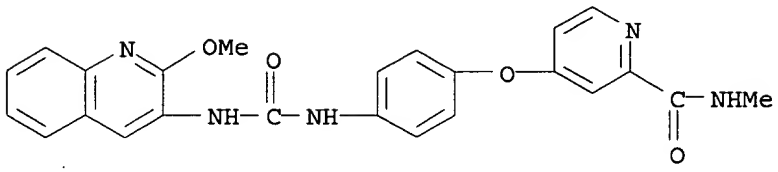
L3 ANSWER 2 OF 8 USPATFULL
AB This invention relates to the use of a group of heteroaryl ureas containing nitrogen in treating p38 mediated diseases, and pharmaceutical compositions for use in such therapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:126779 USPATFULL
TI Heteroaryl ureas containing nitrogen hetero-atoms as p38 kinase inhibitors
IN Dumas, Jacques, Orange, CT, UNITED STATES
Riedl, Bernd, Wuppertal, GERMANY, FEDERAL REPUBLIC OF
Khire, Uday, Hamden, CT, UNITED STATES
Sibley, Robert N., North Haven, CT, UNITED STATES
Hatoum-Mokdad, Holia, Hamden, CT, UNITED STATES
Monahan, Mary-Katherine, Hamden, CT, UNITED STATES
Gunn, David E., Hamden, CT, UNITED STATES
Lowinger, Timotthy B., Nishinomiya City, JAPAN
Scott, William J., Guilford, CT, UNITED STATES

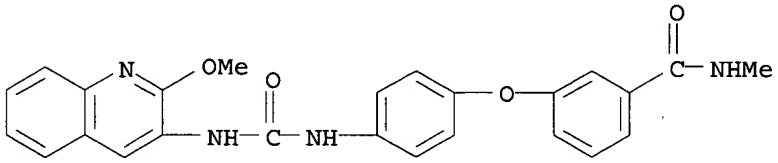
Smith, Roger A., Madison, CT, UNITED STATES
Wood, Jill E., Hamden, CT, UNITED STATES
PA BAYER CORPORATION (U.S. corporation)
PI US 2002065296 A1 20020530
AI US 2001-838286 A1 20010420 (9)
RLI Continuation-in-part of Ser. No. US 2001-778039, filed on 7 Feb 2001, PENDING Continuation-in-part of Ser. No. US 1999-425229, filed on 22 Oct 1999, PENDING Continuation of Ser. No. US 1999-257265, filed on 25 Feb 1999, ABANDONED
PRAI US 1999-115878P 19990113 (60)
DT Utility
FS APPLICATION
LREP MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201
CLMN Number of Claims: 39
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2826
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **432050-20-9P 432050-22-1P**, N-(2-Methoxy-3-quinolinyl)-N'-[4-(2-(N-Methylcarbamyl)-4-pyridyloxy)phenyl]urea **432050-23-2P**, N-(2-Methoxy-3-quinolyl)-N'-[4-[3-(N-methylcarbamoyl)phenoxy]phenyl]urea **432050-24-3P**, N-(2-Methoxy-3-quinolyl)-N'-[4-(2-carbamoyl-4-pyridyloxy)phenyl]urea **432050-25-4P**, N-(2-Methoxy-3-quinolyl)-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea **432050-26-5P**, N-(2-Methoxy-3-quinolyl)-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl]urea **432050-27-6P**, N-(2-Methoxy-3-quinolyl)-N'-[4-[3-(N-isopropylcarbamoyl)phenoxy]phenyl]urea **432050-28-7P**, N-(2-Methoxy-3-quinolyl)-N'-[4-[4-methoxy-3-(N-methylcarbamoyl)phenoxy]phenyl]urea **432050-29-8P**, N-(3-Isoquinolyl)-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea **432050-33-4P**, N-(4-tert-Butyl-2-pyridinyl)-N'-[4-(4-methoxyphenoxy)phenyl]urea **432050-41-4P**, N-(4-tert-Butyl-2-pyridyl)-N'-(4-(4-methylphenoxy)phenyl)urea **432050-42-5P**, N-(4-tert-Butyl-2-pyridyl)-N'-(4-(4-pyridyloxy)phenyl)urea **432050-45-8P 432050-48-1P 432050-52-7P**, N-(Isoquinol-3-yl)-N'-(4-(3-(methylcarbamoyl)phenoxy)phenyl)urea **432050-53-8P**
(prepn. of heteroaryl ureas contg. nitrogen hetero-atoms as p38 kinase inhibitors)
RN 432050-20-9 USPATFULL
CN Urea, N-[4-(4-chlorophenoxy)phenyl]-N'-[4-(1,1-dimethylethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



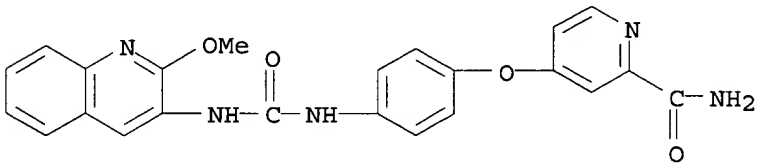
RN 432050-22-1 USPATFULL
CN 2-Pyridinecarboxamide, 4-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



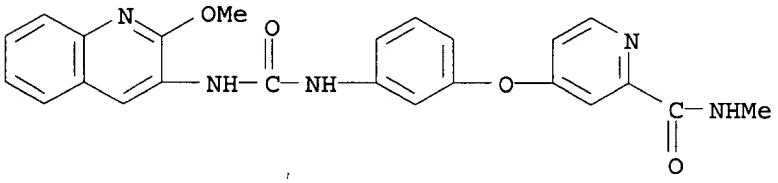
RN 432050-23-2 USPATFULL
CN Benzamide, 3-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



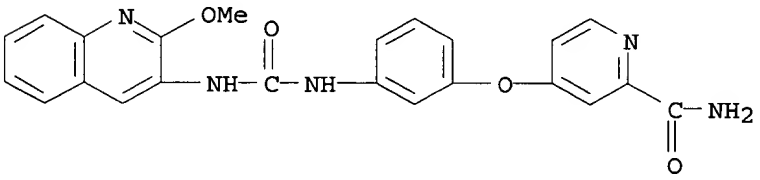
RN 432050-24-3 USPATFULL
CN 2-Pyridinecarboxamide, 4-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



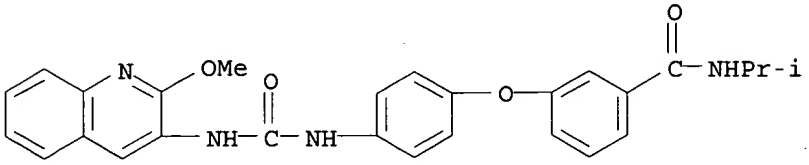
RN 432050-25-4 USPATFULL
CN 2-Pyridinecarboxamide, 4-[3-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



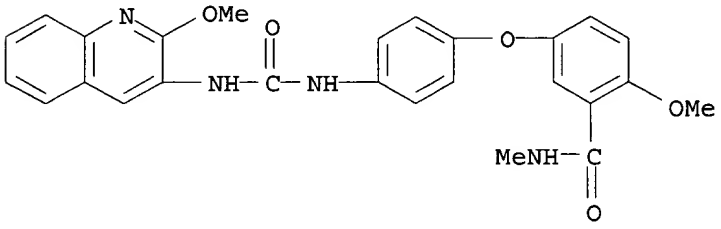
RN 432050-26-5 USPATFULL
CN 2-Pyridinecarboxamide, 4-[3-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



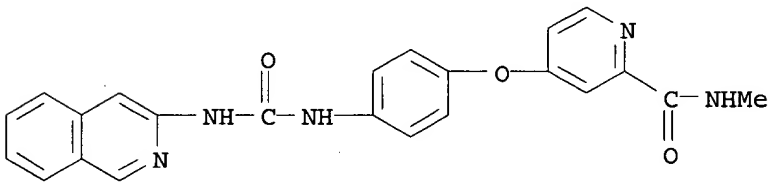
RN 432050-27-6 USPATFULL
CN Benzamide, 3-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



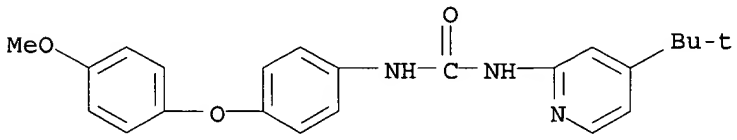
RN 432050-28-7 USPATFULL
CN Benzamide, 2-methoxy-5-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



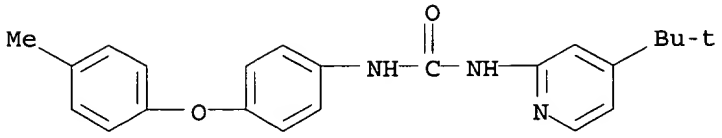
RN 432050-29-8 USPATFULL
CN 2-Pyridinecarboxamide, 4-[4-[[(3-isoquinolinylamino)carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



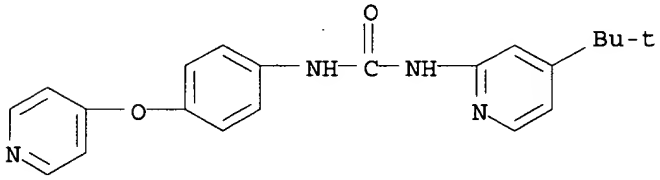
RN 432050-33-4 USPATFULL
CN Urea, N-[4-(1,1-dimethylethyl)-2-pyridinyl]-N'-[4-(4-methoxyphenoxy)phenyl]- (9CI) (CA INDEX NAME)



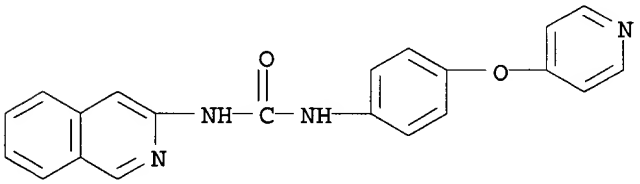
RN 432050-41-4 USPATFULL
CN Urea, N-[4-(1,1-dimethylethyl)-2-pyridinyl]-N'-[4-(4-methylphenoxy)phenyl]- (9CI) (CA INDEX NAME)



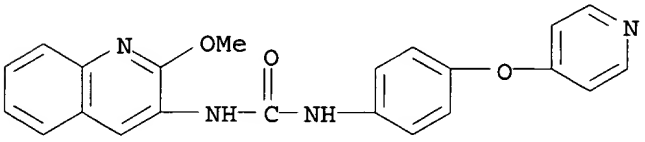
RN 432050-42-5 USPATFULL
CN Urea, N-[4-(1,1-dimethylethyl)-2-pyridinyl]-N'-[4-(4-pyridinyloxy)phenyl]- (9CI) (CA INDEX NAME)



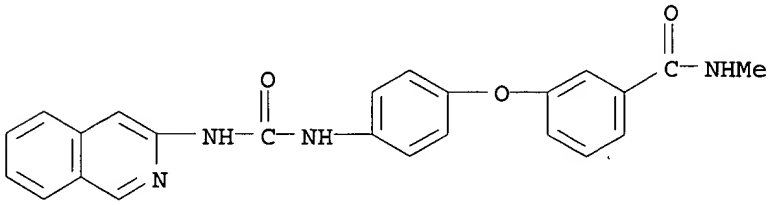
RN 432050-45-8 USPATFULL
CN Urea, N-3-isoquinolinyl-N'-[4-(4-pyridinyloxy)phenyl]- (9CI) (CA INDEX NAME)

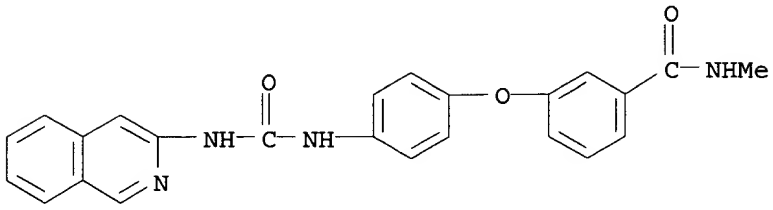


RN 432050-48-1 USPATFULL
CN Urea, N-(2-methoxy-3-quinolinyl)-N'-[4-(4-pyridinyloxy)phenyl]- (9CI) (CA INDEX NAME)

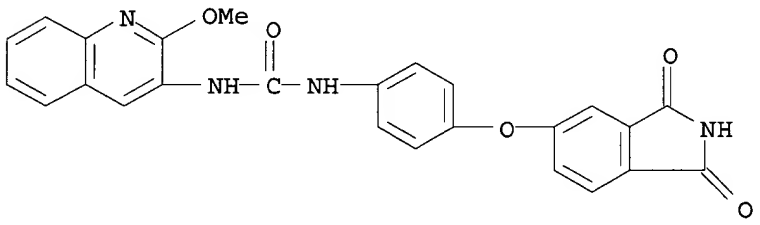


RN 432050-52-7 USPATFULL
CN Benzamide, 3-[4-[[(3-isoquinolinylamino)carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)





RN 432050-53-8 USPATFULL
CN Urea, N-[4-[(2,3-dihydro-1,3-dioxo-1H-isoindol-5-yl)oxy]phenyl]-N'-(2-methoxy-3-quinolinyl)- (9CI) (CA INDEX NAME)

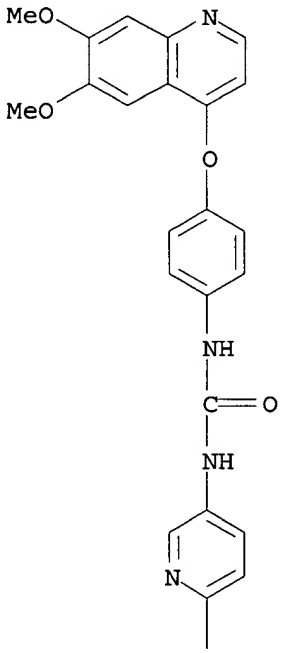


L3 ANSWER 3 OF 8 USPATFULL
AB The present invention relates to novel quinoline derivatives and quinazoline derivatives represented by the following formula (I): ##STR1## [wherein R.sub.1 and R.sub.2 are each independently H or C.sub.1 -C.sub.4 -alkyl, or R.sub.1 and R.sub.2 together form C.sub.1 -C.sub.3 -alkylene, X is O, S or CH.sub.2, W is CH or N, and Q is a substituted aryl group or substituted heteroaryl group] and their pharmaceutically acceptable salts, having platelet-derived growth factor receptor autophosphorylation inhibitory activity, to pharmaceutical compositions containing these compounds, and to methods for the treatment of diseases associated with abnormal cell growth such as tumors.

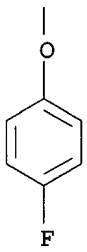
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2000:150184 USPATFULL
TI Quinoline and quinazoline derivatives inhibiting platelet-derived growth factor receptor autophosphorylation and pharmaceutical compositions containing the same
IN Kubo, Kazuo, Takasaki, Japan
Ohyama, Shinichi, Takasaki, Japan
Shimizu, Toshiyuki, Takasaki, Japan
Nishitoba, Tsuyoshi, Takasaki, Japan
Kato, Shinichiro, Takasaki, Japan
Murooka, Hideko, Takasaki, Japan
Kobayashi, Yoshiko, Takasaki, Japan
PA Kirin Beer Kabushiki Kaisha, Tokyo-to, Japan (non-U.S. corporation)
PI US 6143764 20001107
WO 9717329 19970515
AI US 1998-68660 19980506 (9)
WO 1996-JP3229 19961105
19980506 PCT 371 date
19980506 PCT 102(e) date
PRAI JP 1995-313555 19951107
JP 1996-62121 19960223

DT Utility
FS Granted
EXNAM Primary Examiner: Seaman, D. Margaret
LREP Foley & Lardner
CLMN Number of Claims: 52
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5569
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **190727-92-5P**
(prepn. of quinoline and quinazoline derivs. inhibiting platelet-derived growth factor receptor autophosphorylation)
RN 190727-92-5 USPATFULL
CN Urea, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-[6-(4-fluorophenoxy)-3-pyridinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L3 ANSWER 4 OF 8 USPATFULL

AB Compounds of general formula (1) ##STR1## are described wherein Y is a halogen atom or a group --OR.sup.1, where R.sup.1 is an optionally substituted alkyl group; X is --O--, --S-- or --N(R.sup.7)--, where R.sup.7 is a hydrogen atom or an alkyl group; R.sup.2 is an optionally substituted cycloalkyl or cycloalkenyl group; R.sup.3 and R.sup.4, which may be the same or different, is each a hydrogen atom or an alkyl, --CO.sub.2 R.sup.8 (where R.sup.8 is a hydrogen atom or an alkyl, aryl, or aralkyl group), --CONR.sup.9 R.sup.10 (where R.sup.9 and R.sup.10 which may be the same or different is each a hydrogen atom or an alkyl, aryl or aralkyl group), --CSNR.sup.9 R.sup.10, --CN, --CH.sub.2 CN group; Z is --(CH.sub.2).sub.n -- (where n is zero or an integer 1, 2 or 3; R.sup.5 is an optionally substituted monocyclic or bicyclic aryl group optionally containing one or more heteroatoms selected from oxygen, sulphur or nitrogen atoms; R.sup.6 is a hydrogen atom or a hydroxyl group; and the salts, solvates, hydrates, prodrugs and N-oxides thereof. Compounds according to the invention are potent and selective phosphodiesterase type IV inhibitors and are useful in the prophylaxis and treatment of diseases such as asthma where an unwanted inflammatory response or muscular spasm is present.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AN 1999:121385 USPATFULL

TI Trisubstituted phenyl derivatives and processes for their preparation

IN Warrellow, Graham John, Middlesex, United Kingdom HA6 3QU
Cole, Valerie Anne, Buckinghamshire, United Kingdom SL1 7NH
Alexander, Rikki Peter, Buckinghamshire, United Kingdom HP12 3HY

PA Celltech Therapeutics, Limited, Berkshire, United Kingdom (non-U.S. corporation)

PI US 5962483 19991005

AI US 1998-8173 19980116 (9)

RLI Division of Ser. No. US 1995-543962, filed on 17 Oct 1995, now patented, Pat. No. US 5739144 which is a continuation of Ser. No. US 1995-384612, filed on 2 Feb 1995, now abandoned which is a continuation of Ser. No. US 1994-208656, filed on 9 Mar 1994, now abandoned

PRAI GB 1993-4920 19930310

DT Utility

FS Granted

EXNAM Primary Examiner: Davis, Zinna Northington

LREP Woodcock Washburn Kurtz Mackiewicz & Norris LLP

CLMN Number of Claims: 20

ECL Exemplary Claim: 1

DRWN No Drawings

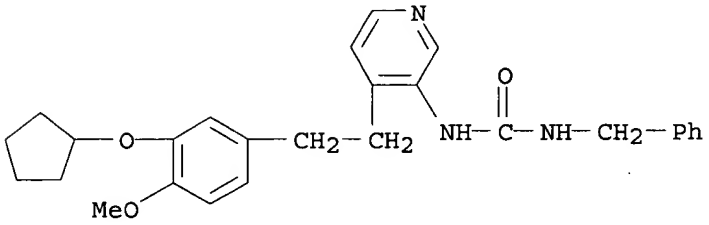
LN.CNT 1701

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **159196-19-7P**
(prepn. of heterocyclic trisubstituted Ph derivs. as phosphodiesterase inhibitors)

RN 159196-19-7 USPATFULL

CN Urea, N-[4-[2-[3-(cyclopentyloxy)-4-methoxyphenyl]ethyl]-3-pyridinyl]-N'-(phenylmethyl)- (9CI) (CA INDEX NAME)



L3 ANSWER 5 OF 8 USPATFULL

AB This invention is directed to the pharmaceutical use of phenyl compounds, which are linked to an aryl moiety by various linkages, for inhibiting tumor necrosis factor. The invention is also directed to the compounds, their preparation and pharmaceutical compositions containing these compounds. Furthermore, this invention is directed to the pharmaceutical use of the compounds for inhibiting cyclic AMP phosphodiesterase.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AN 1999:92693 USPATFULL

TI Compounds containing phenyl linked to aryl or heteroaryl by an aliphatic- or heteroatom-containing linking group

IN Fenton, Garry, Dagenham, United Kingdom
Morley, Andrew David, Dagenham, United Kingdom
Palfreyman, Malcolm Norman, Dagenham, United Kingdom
Ratcliffe, Andrew James, Dagenham, United Kingdom
Sharp, Brian William, Dagenham, United Kingdom
Thurairatnam, Sukanthini, Dagenham, United Kingdom
Vacher, Bernard Yvon Jack, Dagenham, United Kingdom
Ashton, Michael John, Dagenham, United Kingdom
Cook, David Charles, Dagenham, United Kingdom
Hills, Susan Jacqueline, Dagenham, United Kingdom
McFarlane, Ian Michael, Dagenham, United Kingdom
Vicker, Nigel, Dagenham, United Kingdom

PA Rhone-Poulenc Rorer Limited, West Malling, United Kingdom (non-U.S. corporation)

PI US 5935978 19990810

AI US 1993-98178 19930728 (8)

RLI Continuation-in-part of Ser. No. WO 1992-GB153, filed on 28 Jan 1992, now abandoned

PRAI GB 1991-1777 19910128
GB 1991-17727 19910816
GB 1992-15989 19920728
GB 1992-16005 19920728
GB 1992-16006 19920728
GB 1992-16008 19920728
GB 1992-16764 19920807
GB 1993-10633 19930521
GB 1993-10938 19930527
GB 1993-11281 19930601
GB 1993-14847 19930716

DT Utility

FS Granted

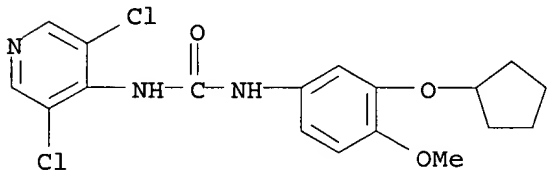
EXNAM Primary Examiner: Davis, Zinna Northington

LREP Parker, III, Raymond S., Savitzky, Martin F.

CLMN Number of Claims: 36

ECL Exemplary Claim: 1

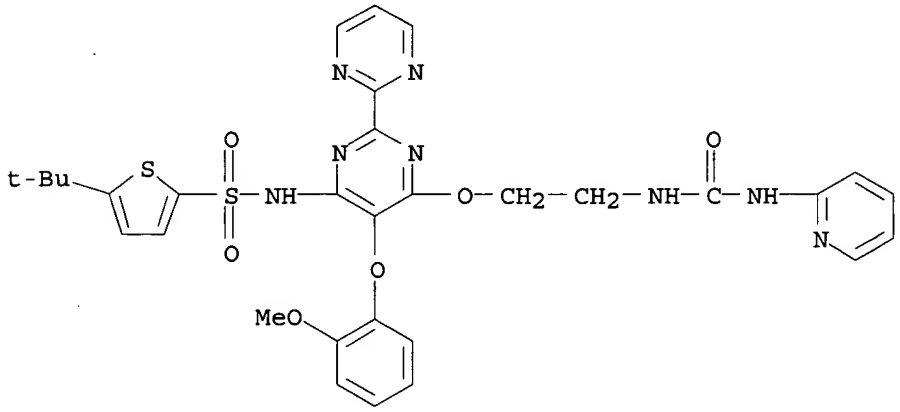
DRWN No Drawings
LN.CNT 4870
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **159782-49-7P**, N-(3,5-Dichloropyrid-4-yl)-N'-(3-cyclopentyloxy-4-methoxyphenyl)urea
(prepn. of N-(hetero)aryl 3,4-(cyclo)alkoxybenzamides and analogs useful as tumor necrosis factor and c-AMP phosphodiesterase inhibitors)
RN 159782-49-7 USPATFULL
CN Urea, N-[3-(cyclopentyloxy)-4-methoxyphenyl]-N'-(3,5-dichloro-4-pyridinyl)- (9CI) (CA INDEX NAME)



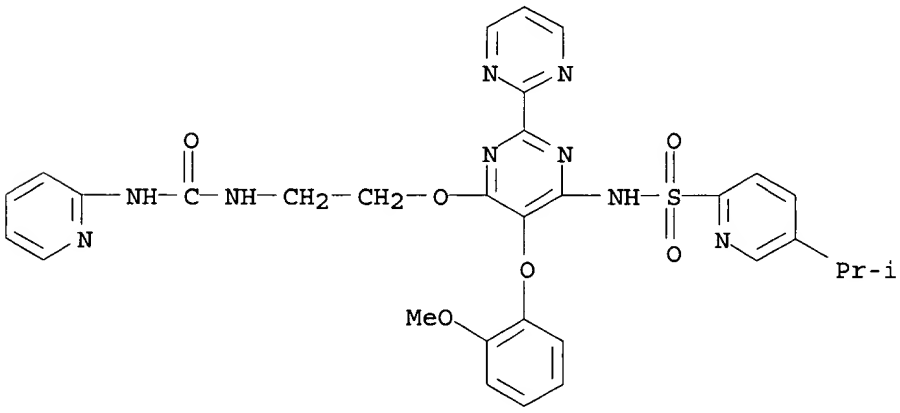
L3 ANSWER 6 OF 8 USPATFULL
AB Compounds of the formula ##STR1## wherein the variables are hereinbelow defined. The compounds of formula I are inhibitors for endothelin receptors. They can be used for the treatment of disorders which are associated with endothelin activities, especially circulatory disorders such as hypertension, ischaemia, vasospasms and angina pectoris.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 1998:144107 USPATFULL
TI Sulphonamides
IN Breu, Volker, Schliengen, Germany, Federal Republic of
Burri, Kaspar, Binningen, Switzerland
Cassal, Jean-Marie, Mulhouse, France
Clozel, Martine, St. Louis, France
Hirth, Georges, Huningue, France
Loffler, Bernd-Michael, Oberrimsingen, Germany, Federal Republic of
Muller, Marcel, Frenkendorf, Switzerland
Neidhart, Werner, Hagenthal le Bas, France
Ramuz, Henri, Birsfelden, Switzerland
PA Hoffmann-La Roche Inc., Nutley, NJ, United States (U.S. corporation)
PI US 5837708 19981117
AI US 1996-730422 19961015 (8)
RLI Continuation-in-part of Ser. No. US 1996-676313, filed on 18 Jul 1996
PRAI CH 1994-3559 19941125
WO 1995-CH131 19950606
DT Utility
FS Granted
EXNAM Primary Examiner: Ford, John M.
LREP Johnston, George W., Epstein, William H., Parise, John P.
CLMN Number of Claims: 39
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1715
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **179400-23-8P 179400-32-9P**
(prepn. of N-(phenoxypyrimidinyl)heteroarom. sulfonamides as endothelin antagonists)
RN 179400-23-8 USPATFULL

CN 2-Thiophenesulfonamide, 5-(1,1-dimethylethyl)-N-[5-(2-methoxyphenoxy)-6-[2-[[(2-pyridinylamino)carbonyl]amino]ethoxy][2,2'-bipyrimidin]-4-yl]-(9CI) (CA INDEX NAME)



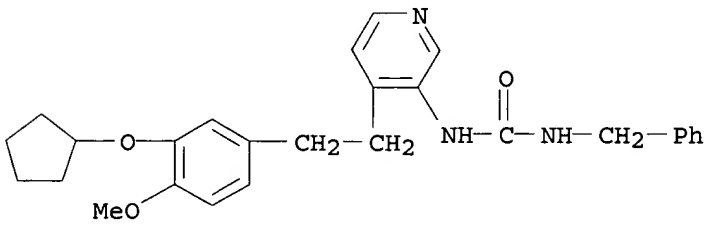
RN 179400-32-9 USPATFULL
CN 2-Pyridinesulfonamide, N-[5-(2-methoxyphenoxy)-6-[2-[[(2-pyridinylamino)carbonyl]amino]ethoxy][2,2'-bipyrimidin]-4-yl]-5-(1-methylethyl)- (9CI) (CA INDEX NAME)



L3 ANSWER 7 OF 8 USPATFULL
AB Compounds of general formula (1) ##STR1## are described wherein Y is a halogen atom or a group --OR.sup.1, where R.sup.1 is an optionally substituted alkyl group; X is --O--, --S-- or --N(R.sup.7)--, where R.sup.7 is a hydrogen atom or an alkyl group; R.sup.2 is an optionally substituted cycloalkyl or cycloalkenyl group; R.sup.3 and R.sup.4, which may be the same or different, is each a hydrogen atom or an alkyl, --CO.sub.2 R.sup.8 (where R.sup.8 is a hydrogen atom or an alkyl, aryl, or aralkyl group), --CONR.sup.9 R.sup.10 (where R.sup.9 and R.sup.10 which may be the same or different is each a hydrogen atom or an alkyl, aryl or aralkyl group), --CSNR.sup.9 R.sup.10, --CN, --CH.sub.2 CN group; Z is --(CH.sub.2).sub.n -- (where n is zero or an integer 1, 2 or 3; R.sup.5 is an optionally substituted monocyclic or bicyclic aryl

group optionally containing one or more heteroatoms selected from oxygen, sulphur or nitrogen atoms; R.sup.6 is a hydrogen atom or a hydroxyl group; and the salts, solvates, hydrates, prodrugs and N-oxides thereof. Compounds according to the invention are potent and selective phosphodiesterase type IV inhibitors and are useful in the prophylaxis and treatment of diseases such as asthma where an unwanted inflammatory response or muscular spasm is present.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 1998:39535 USPATFULL
TI Trisubstituted phenyl derivatives
IN Warrellow, Graham John, Northwood, United Kingdom
Cole, Valerie Anne, Burnham, United Kingdom
Alexander, Rikki Peter, High Wycombe, United Kingdom
PA Celltech Therapeutics Limited, Slough, United Kingdom (non-U.S. corporation)
PI US 5739144 19980414
AI US 1995-543962 19951017 (8)
RLI Continuation of Ser. No. US 1995-384612, filed on 2 Feb 1995, now abandoned which is a continuation of Ser. No. US 1994-208656, filed on 9 Mar 1994, now abandoned
PRAI GB 1993-4920 19930310
DT Utility
FS Granted
EXNAM Primary Examiner: Geist, Gary; Assistant Examiner: Keys, Rosalynd
LREP Woodcock Washburn Kurtz Mackiewicz & Norris LLP
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1604
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **159196-19-7P**
(prepn. of heterocyclic trisubstituted Ph derivs. as phosphodiesterase inhibitors)
RN 159196-19-7 USPATFULL
CN Urea, N-[4-[2-[3-(cyclopentyloxy)-4-methoxyphenyl]ethyl]-3-pyridinyl]-N'-(phenylmethyl)- (9CI) (CA INDEX NAME)

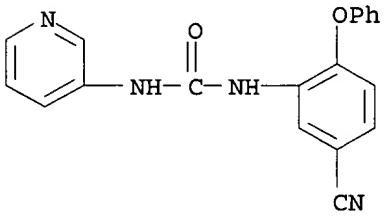


L3 ANSWER 8 OF 8 USPATFULL
AB Compounds having the formula ##STR1## and pharmaceutically acceptable salts thereof wherein X is a single bond, O, CO, S, NH or N(lower alkyl); Y is O, S or NCN; and R.sup.1 to R.sup.5' are as defined herein. These compounds have potassium channel activating activity and are useful, therefore for example, as cardiovascular agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 96:75411 USPATFULL

Print selected from Online session09/09/2002

TI Aryl urea and related compounds
IN Atwal, Karnail S., Newtown, PA, United States
Ferrara, Francis N., Martinsville, NJ, United States
Ding, Charles Z., Plainsboro, NJ, United States
PA Bristol-Myers Squibb Company, Princeton, NJ, United States (U.S. corporation)
PI US 5547966 19960820
AI US 1993-134195 19931007 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Gupta, Yogendra N.
LREP Park, Ellen K.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 911
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **166263-16-7P**
(prepn. of biaryl ureas and analogs as cardiovascular agents)
RN 166263-16-7 USPATFULL
CN Urea, N-(5-cyano-2-phenoxyphenyl)-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



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L4           26 L2

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             26 L2
L5            0 L4 NOT L3

=> d his

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GI
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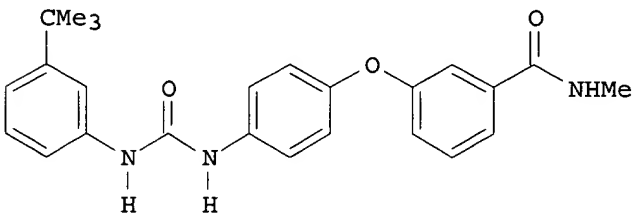


II

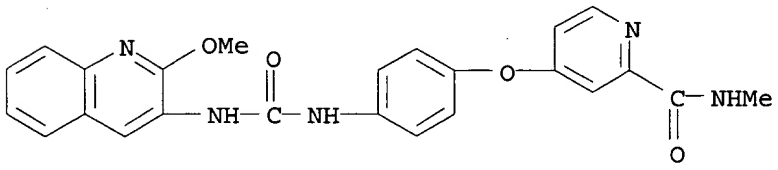
AB Title compds., e.g., RNHCONHZOR1 [I; R = C6H4(CMe3)-3, 2-methoxy-5-trifluoromethylphenyl, 4-chloro-3-trifluoromethylphenyl, 2-methoxy-3-quinolyl, etc.; R1 = (un)substituted acylphenyl, -acylpyridinyl, etc.; Z = (un)substituted 1,3- or -1,4-phenylene] were prepd. Thus, 4-(H2N)C6H4OC6H4(CONHMe)-4 (prepn. given) was condensed with 3-(Me3C)C6H4NH2 and CO(OCCl3)2 to give title compd. II. Data for biol. activity of title compds. were given.

AN 2002:615574 CAPLUS
TI Preparation of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors
IN Dumas, Jacques; Riedl, Bernd; Khire, Uday; Wood, Jill E.; Sibley, Robert N.; Monahan, Mary-Katherine; Renick, Joel; Gunn, David E.; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.
PA Bayer Corporation, USA
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062763	A2	20020815	WO 2002-US203361	20020207

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-777920 A 20010207
IT **432050-22-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors)
RN 432050-22-1 CAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)

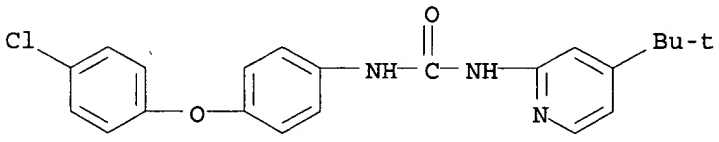


L4 ANSWER 2 OF 26 CAPLUS COPYRIGHT 2002 ACS
AB This invention relates to the use of a group of heteroaryl ureas (I; for example, N-(2-methoxy-3-quinolyl)-N'-[4-[3-(N-methylcarbamoyl)phenoxy]phenyl]urea) contg. N in treating p38 mediated diseases, and pharmaceutical compns. for use in such therapy. I is A-NHC(O)NH-B or a pharmaceutically acceptable salt thereof, wherein A is a substituted or unsubstituted pyridyl, quinolinyl or isoquinolinyl group, B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 50 C atoms with a cyclic structure bound directly to N, contg. at least 5 cyclic members with 0-4 members of groups consisting of N, O and S. Information about the substituents for A and B are given in the claims. Although the methods of prepn. are not claimed, 37 example prepns. are included as well as examples of prepn. of intermediates. No pharmacol. data is included.

AN 2002:409267 CAPLUS
DN 137:6098
TI Heteroaryl ureas containing nitrogen hetero-atoms as p38 kinase inhibitors
IN Dumas, Jacques; Riedl, Bernd; Khire, Uday; Sibley, Robert N.; Hatoum-Mokdad, Holia; Monahan, Mary-katherine; Gunn, David E.; Lowinger, Timotthy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.
PA Bayer Corporation, USA
SO U.S. Pat. Appl. Publ., 39 pp., Cont.-in-part of U. S. Ser. No. 778,039.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

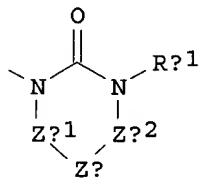
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2002065296	A1	20020530	US 2001-838286	20010420
PRAI US 1999-115878P	P	19990113		
US 1999-257265	B1	19990225		
US 1999-425229	A2	19991022		
US 2001-778039	A2	20010207		

OS MARPAT 137:6098
IT **432050-20-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heteroaryl ureas contg. nitrogen hetero-atoms as p38 kinase inhibitors)
RN 432050-20-9 CAPLUS
CN Urea, N-[4-(4-chlorophenoxy)phenyl]-N'-[4-(1,1-dimethylethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 3 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI

Q=



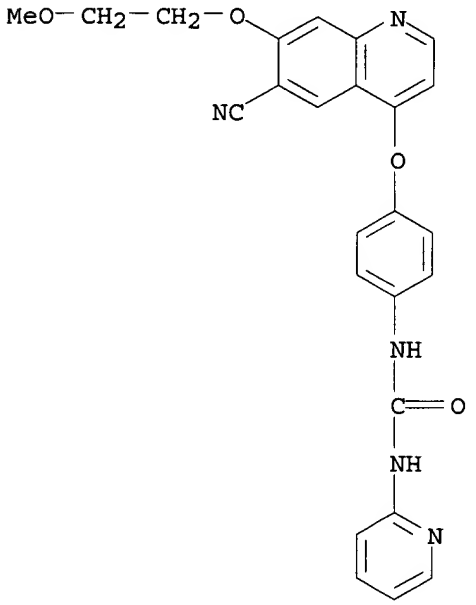
AB N-aryl or N-heteroarylurea derivs. represented by the general formula Ag-Xg-Yg-Tg1 or salts thereof, or hydrates of both [wherein Ag = (un)substituted C6-14 aryl or 5- to 14-membered heterocyclic group; Xg = single bond, O, S, C1-6 alkylene, SO, SO2, (un)substituted NH; Yg = (un)substituted C6-14 aryl, 5- to 14-membered heterocyclic group, C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl-C1-6 alkyl, 5- to

14-membered heteroaryl-C1-6 alkyl, (CH2)gSO2 (g = 1-8), (CH2)faCH:CH(CH2)fb (fa, fb = 0, 1,2,3), etc.; and Tg1 = a group of the general formula -Eg-CO-NRg1(Zg) or Q; wherein Eg = a single bond, (un)substituted NH; Rg1 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-8 aliph. hydrocarbyl, etc.; Zg = C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl, etc.; Zg1, Zg2 = (a) a single bond, (b) C1-6 alkylene optionally having .gtoreq.1 atoms selected from O, S, and N in the middle or the terminus of the chain and optionally substituted with oxo, (c) (un)substituted C2-6 alkenyl] are prepd. These compds. are also inhibitors of vascular endothelial growth factor receptor kinase (VEGFR2 kinase) and are useful as antitumor agents against hemangioma, pancreatic cancer, stomach cancer, colon cancer, breast cancer, prostate cancer, lung cancer, brain tumor, leukemia, or ovarian cancer, as cancer metastasis inhibitors, and for the treatment of retina neovascularization, diabetic retinopathy, atherosclerosis, or inflammatory diseases such as osteoarthritis, rheumatoid arthritis, psoriasis, or delayed hypersensitivity. Thus, to soln. of 334 mg 4-[6-(4-benzyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenylamine in 4 mL DMF were added 0.066 mL pyridine and 0.102 mL Ph chlorocarbonate and stirred at room temp. for 2.5 h to give 330 mg N-[4-[6-(4-benzyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropylurea which (260 mg) was hydrogenolyzed over platinum oxide in ethanol overnight to give 160 mg N-[4-[6-(4-hydroxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropylurea (I). I showed IC50 of 0.02 nM for inhibiting the vascular endothelial growth factor (VEGF)-stimulated sandwich tube formation in vascular endothelial cell.

AN 2002:314913 CAPLUS
DN 136:340689
TI Preparation of urea derivatives containing nitrogenous aromatic ring compounds as inhibitors of angiogenesis
IN Funahashi, Yasuhiro; Tsuruoka, Akihiko; Matsukura, Masayuki; Haneda, Toru; Fukuda, Yoshio; Kamata, Junichi; Takahashi, Keiko; Matsushima, Tomohiro; Miyazaki, Kazuki; Nomoto, Kenichi; Watanabe, Tatsuo; Obaishi, Hiroshi; Yamaguchi, Atsumi; Suzuki, Sachi; Nakamura, Katsuji; Mimura, Fusayo; Yamamoto, Yuji; Matsui, Junji; Matsui, Kenji; Yoshiba, Takako; Suzuki, Yasuyuki; Arimoto, Itaru
PA Eisai Co., Ltd., Japan
SO PCT Int. Appl., 699 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

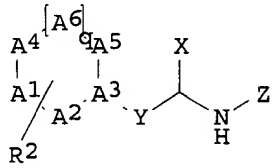
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002032872	A1	20020425	WO 2001-JP9221	20011019
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	JP 2000-320420	A	20001020		
	JP 2000-386195	A	20001220		
	JP 2001-46685	A	20010222		

OS MARPAT 136:340689
IT **417712-95-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of urea derivs. contg. nitrogenous arom. ring compds. as angiogenesis inhibitors for prevention or treatment of diseases)
RN 417712-95-9 CAPLUS
CN Urea, N-[4-[[6-cyano-7-(2-methoxyethoxy)-4-quinolinyl]oxy]phenyl]-N'-2-pyridinyl- (9CI) (CA INDEX NAME)



RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI



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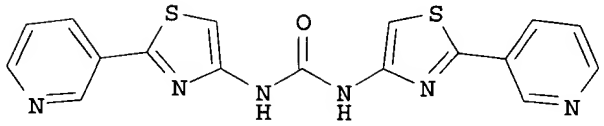


II

AB The title compds. [I; A1-A6 = CH2, CH, C, O, S, Nh, N; X and Z taken together to form a N atom contg. ring; Y = NHCO(CH2)p, CH2CO2, NHSO2CH2, NHCO2, NHCONR6(CH2)r; R2 = alkylaminoalkynyl, cycloalkenylalkynyl, phenylalkynyl, etc.; p = 1-2; q = 0-1; r = 0-3; R6 is not defined] which are effective for prophylaxis and treatment of diseases, such as cell proliferation or apoptosis mediated diseases involving stroke, cancer and the like, were prepd. Thus, treating 3-(3-pyridyl)-4-thiazolylcarbonylazide in PhMe with a few drops of H2O afforded the urea II which showed cdk2/cyclin and cdk5/cyclin kinase activity with IC50 of < 50 .mu.M.

AN 2002:142704 CAPLUS

DN 136:200177

TI Preparation of diheteroaryl ureas as antitumor agents

IN Santora, Vent; Askew, Benny; Ghose, Arup; Hague, Andrew; Kim, Tae Seong; Laber, Ellen; Li, Aiwen; Lian, Brian; Liu, Gang; Norman, Mark Henry; Smith, Leon; Tasker, Andrew; Tegley, Christopher; Yang, Kevin

PA Amgen Inc., USA

SO PCT Int. Appl., 371 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

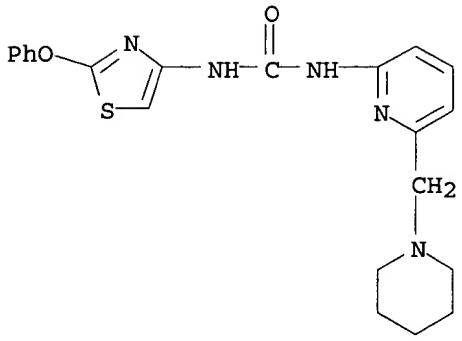
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002014311	A2	20020221	WO 2001-US25472	20010815
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001084909	A5	20020225	AU 2001-84909	20010815
PRAI	US 2000-225793P	P	20000815		
	WO 2001-US25472	W	20010815		

OS MARPAT 136:200177

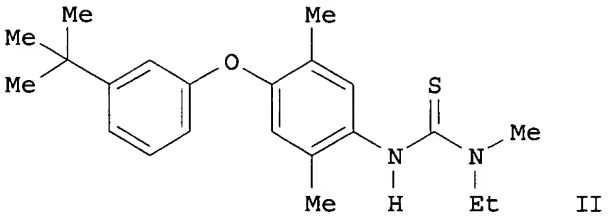
IT **400773-51-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of diheteroaryl ureas as antitumor agents)

RN 400773-51-5 CAPLUS

CN Urea, N-(2-phenoxy-4-thiazolyl)-N'-[6-(1-piperidinylmethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



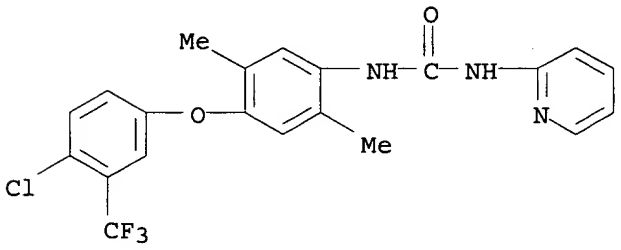
L4 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI



AB R6ZZ1NRC(:X)R5 [I; R = H, alkyl, etc.; R5 = NR1R2, OR3, SR3; R1,R2 = H, alkyl, acyl, etc.; RR1, RR3, R1R2 = atoms to complete a ring; R3 = H, alkyl, etc.; R6 = 2-benzothienyl, 5-tert-butyl-1,3,4-oxadiazol-2-yl, substituted Ph, etc.; X = O or S; Z = bond, O, CO, SO0-2, NH, etc.; Z1 = e.g., 2,5-dimethyl-1,4-phenylene] were prepd. Thus, 2-chloro-1,4-xylene was nitrated and the product etherified by 3-(Me3C)C6H4OH to give, after redn., the phenoxyanilline which was treated with Cl2CS and the product amidated by HNMeEt to give title compd. II. Data for biol. activity of I were given.
AN 2002:104657 CAPLUS
DN 136:151003
TI Preparation of N-[(aryloxy)phenyl](thio)ureas and -carbamates as agrochemical fungicides
IN Gerusz, Vincent; Mansfield, Darren James; Perez, Jose; Tickle, David; Vors, Jean-Pierre; Baldwin, Derek; Hough, Thomas; Mitchell, Dale Robert
PA Aventis Cropscience S.A., Fr.
SO Eur. Pat. Appl., 42 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

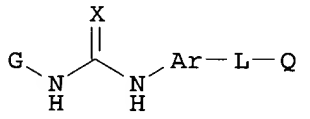
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1178039	A1	20020206	EP 2001-420173	20010801
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
FR 2812633	A1	20020208	FR 2000-10305	20000804

JP 2002114751 A2 20020416 JP 2001-238513 20010806
PRAI FR 2000-10305 A 20000804
OS MARPAT 136:151003
IT **395658-94-3P**
RL: AGR (Agricultural use); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-[(aryloxy)phenyl](thio)ureas and -carbamates as agrochem. fungicides)
RN 395658-94-3 CAPLUS
CN Urea, N-[4-[4-chloro-3-(trifluoromethyl)phenoxy]-2,5-dimethylphenyl]-N'-2-pyridinyl- (9CI) (CA INDEX NAME)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI



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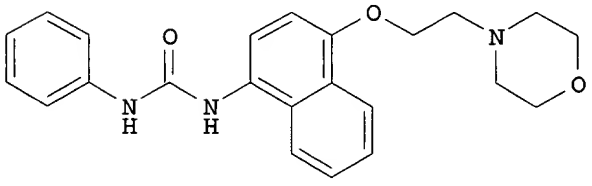


II

AB Title compds. (I) [wherein G = (un)substituted (non)arom. carbocycle or heterocycle; Ar = (un)substituted Ph, (tetrahydro)naphthyl, (tetrahydro)quinolinyl, (tetrahydro)isoquinolinyl, (dihydro)benzofuranyl, dihydrobenzothienyl, indolenyl, benzothiophenyl, benzimidazolyl, indanyl, indenyl, or indolyl; L = (un)substituted (un)satd. C chain with one or more methylene groups optionally independently replaced by O, N, or S(O)m; Q = (un)substituted Ph, naphthyl, pyridinyl, pyrimidinyl, pyridazinyl, (benz)imidazolyl, furanyl, thenyl, pyranyl, etc.; m = 0-2; X = O or S] were prepd. as cytokine prodn. inhibitors for use as non-steroidal anti-inflammatory agents. Thus, 4-[2-(morpholin-4-yl)ethoxy]naphth-1-

ylamine was treated sequentially with phosgene and 5-tert-butyl-2-methylaniline in CH2Cl2 to give II (42%). In a cytokine prodn. inhibition assay, II inhibited TNF.alpha. in lipopolysaccharide stimulated THP cells with IC50 < 10 .mu.M.

AN 2001:380570 CAPLUS

DN 135:5453

TI Preparation of aromatic heterocyclic substituted urea derivatives as non-steroidal anti-inflammatory agents

IN Breitfelder, Steffen; Cirillo, Pier F.; Hao, Ming-Hong; Hickey, Eugene R.; Sharma, Rajiv; Sun, Sanxing; Takahashi, Hidenori

PA Boehringer Ingelheim Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

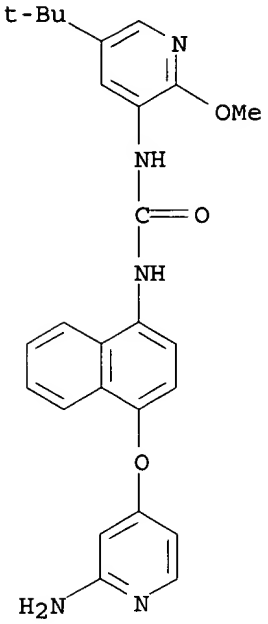
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001036403	A1	20010525	WO 2000-US31582	20001116
	W: AE, AU, BG, BR, BY, CA, CN, CZ, EE, HR, HU, ID, IL, IN, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, VN, YU, ZA				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	EP 1232150	A1	20020821	EP 2000-978751	20001116
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR				
PRAI	US 1999-165903P	P	19991116		
	WO 2000-US31582	W	20001116		

OS MARPAT 135:5453

IT **340825-57-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arom. heterocyclic substituted urea derivs. as cytokine inhibitors for use as non-steroidal anti-inflammatory agents)

RN 340825-57-2 CAPLUS

CN Urea, N-[4-[(2-amino-4-pyridinyl)oxy]-1-naphthalenyl]-N'-[5-(1,1-dimethylethyl)-2-methoxy-3-pyridinyl]- (9CI) (CA INDEX NAME)



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; Z = O, S; R1 = alkyl, alkenyl, alkoxy, etc.; R2-R6 = alkyl, alkenyl, alkoxy, etc.; adjacent pair of R2-R6 together with the carbon atoms to which they are attached form (un)substituted carbocyclyl, heterocyclyl; R7 = alkyl, alkenyl, alkoxy, etc.; n = 0-3] and their pharmaceutically acceptable salts which are non-peptide antagonists of human orexin receptors, in particular orexin-1 receptors, were prepd. E.g., treatment of 4-amino-2-methylquinoline with carbonyl diimidazole in CH2Cl2 followed by addn. of 6-amino-2-methylbenzoxazole afforded II which showed pKb > 6.0 against orexin-1 receptor. In particular, compds. I are of potential use in the treatment of obesity including obesity obsd. in Type 2(non-insulin-dependent) diabetes patients and/or sleep disorders.
AN 2000:573791 CAPLUS
DN 133:164009
TI Preparation of phenyl ureas and thioureas as orexin receptor antagonists
IN Coulton, Steven; Johns, Amanda; Porter, Roderick Alan
PA Smithkline Beecham Plc, UK
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000047577	A1	20000817	WO 2000-EP1150	20000210

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1150977 A1 20011107 EP 2000-906324 20000210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRAI GB 1999-3266 A 19990212
GB 1999-26430 A 19991108
WO 2000-EP1150 W 20000210

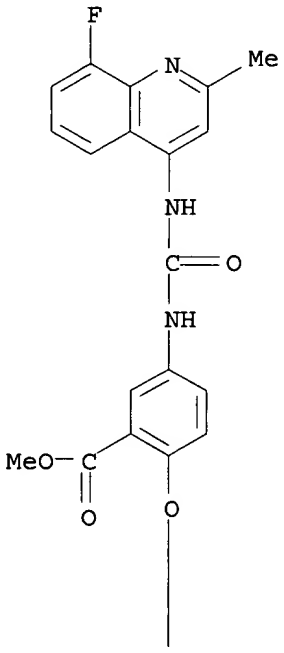
OS MARPAT 133:164009

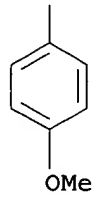
IT **288151-08-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of Ph ureas and thioureas as orexin receptor antagonists)

RN 288151-08-6 CAPLUS

CN Benzoic acid, 5-[[[(8-fluoro-2-methyl-4-quinolinyl)amino]carbonyl]amino]-2-(4-methoxyphenoxy)-, methyl ester (9CI) (CA INDEX NAME)

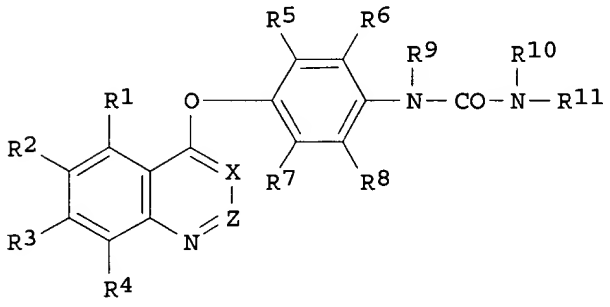
PAGE 1-A





RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI



I

AB Title compds. [I; X and Z represent each CH or N; R1-3 represent each H, optionally substituted alkoxy, etc.; R4 represents H; R5-8 represent each H, halogeno, alkyl, alkoxy, alkylthio, nitro or amino, provided that all of R5-8 do not represent H simultaneously; R9 and R10 represent each H, alkyl or alkylcarbonyl; and R11 represents alkyl, alkenyl, alkynyl or aralkyl], pharmaceutically acceptable salts and solvates, and medicinal compns. contg. the same are prepd. and tested having antitumor activity and causing no morphol. change in cells. Thus, the title compd. I (X = CH; Z = CH; R1, R4, R5,R7-R10 each an H; R11 = 3,5-F2C6H3) was prepd. and tested.

AN 2000:513673 CAPLUS

DN 133:135235

TI Preparation and anti-tumor, anti-atherosclerosis, anti-psoriasis, anti-diabetes, and anti-arthritis activities of quinolines and quinazolines

IN Kubo, Kazuo; Fujiwara, Yasunari; Isoe, Toshiyuki

PA Kirin Beer Kabushiki Kaisha, Japan

SO PCT Int. Appl., 208 pp.
CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

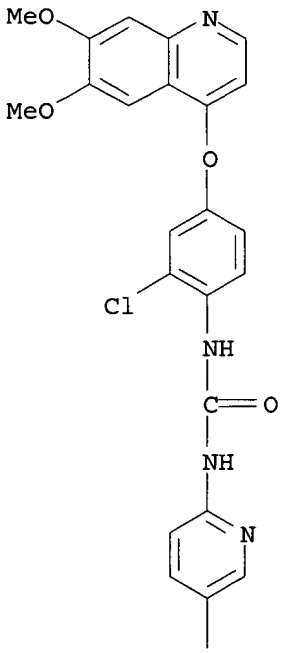
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000043366	A1	20000727	WO 2000-JP255	20000120

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,

MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

BR 2000007656 A 20011030 BR 2000-7656 20000120
EP 1153920 A1 20011114 EP 2000-900841 20000120
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
NO 2001002617 A 20010914 NO 2001-2617 20010529
PRAI JP 1999-14858 A 19990122
JP 1999-26691 A 19990203
JP 1999-142493 A 19990521
JP 1999-253624 A 19990907
WO 2000-JP255 W 20000120
OS MARPAT 133:135235
IT **286369-67-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and antitumor activity of quinolines and quinazolines)
RN 286369-67-3 CAPLUS
CN Urea, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(5-chloro-2-pyridinyl)- (9CI) (CA INDEX NAME)

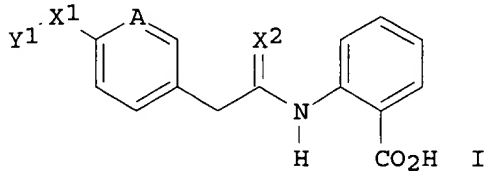
PAGE 1-A



Cl

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI



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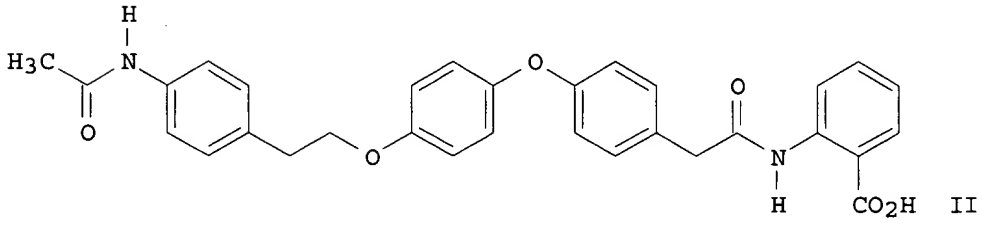


II

AB Title compds. [I; wherein Y1 = a group represented by (un)substituted-Ph, (un)substituted-2-naphthyl; X1 is O, S; X2 is O or S; A = CH, N] and stereoisomers are prepd. and tested as antagonists of IgE antibody, therefore useful as preventive or therapeutic agents for allergic diseases and having cytotoxic activities useful as antitumor agents. The title compd. II was prepd.

AN 2000:84754 CAPLUS
DN 132:151571
TI Preparation of anthranilic acid derivatives as preventive or therapeutic agents
IN Tsuchiya, Naoki; Takeuchi, Susumu; Takeyasu, Takumi; Hase, Naoki; Yamori, Takao; Tsuruo, Takashi
PA Teijin Limited, Japan
SO PCT Int. Appl., 213 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000005198	A1	20000203	WO 1999-JP3969	19990723

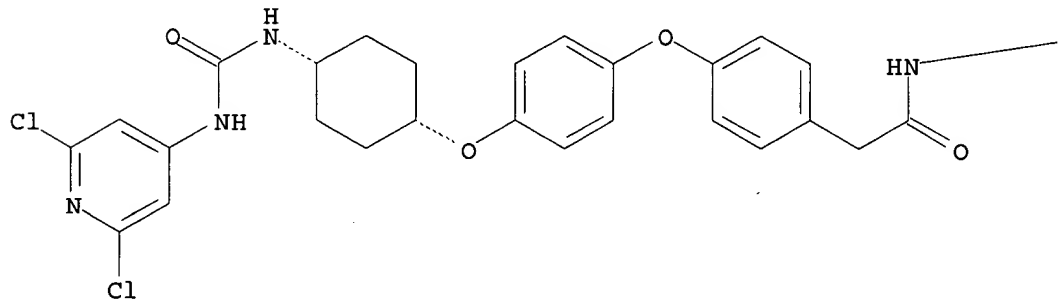
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,

MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

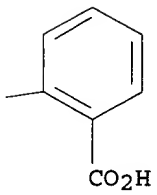
AU 9948004 A1 20000214 AU 1999-48004 19990723
EP 1101755 A1 20010523 EP 1999-931522 19990723
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRAI JP 1998-209410 A 19980724
JP 1998-258486 A 19980911
JP 1998-369808 A 19981225
JP 1998-369809 A 19981225
WO 1999-JP3969 W 19990723
OS MARPAT 132:151571
IT **257606-70-5P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of anthranilic acid derivs. as preventive or therapeutic agents)
RN 257606-70-5 CAPLUS
CN Benzoic acid, 2-[[[4-[4-[[cis-4-[[[(2,6-dichloro-4-pyridinyl)amino]carbonyl]amino]cyclohexyl]oxy]phenoxy]phenyl]acetyl]amino]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 26 CAPLUS COPYRIGHT 2002 ACS
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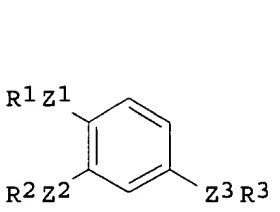

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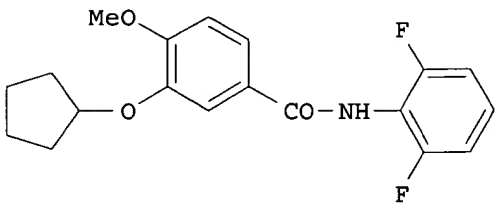


II

AB Title compds. (I) [R1 = lower alkyl; R2 = (un)substituted cycloalkyl, (un)substituted cycloalkenyl, (un)substituted or oxidized cyclothioalkyl, or (un)substituted or oxidized cyclothioalkenyl; R3 = (un)substituted (hetero)aryl; Z, Z1, Z2 = independently O or S; Z3 = C(:Z)NH] and their N-oxides and salts were prepd. for pharmaceutical use as tumor necrosis factor and cAMP phosphodiesterase inhibitors. Thus, 3-cyclopentyloxy-4-methoxybenzoyl chloride (prepn. given) in CH2Cl2 was added dropwise to 2,6-difluoroaniline in triethylamine and CH2Cl2 and refluxed for 4 h to yield N-(2,6-difluorophenyl)-3-cyclopentyloxy-4-methoxybenzamide (II). Compds. of the invention were tested for inhibitory effects on PDE activity and eosinophil superoxide generation, effects on tracheal smooth muscle contractility, in vivo bronchodilator actions and antigen(ovalbamin)-induced eosinophilia, in vitro inhibitory effects on TNF-.alpha. release by human monocytes, and inhibitory effects on antigen-induced bronchoconstriction in conscious guinea-pigs and serum TNF-.alpha. levels in LPS-challenged mice. Compds. showed 10,000-fold to 50-fold more selectivity for cAMP phosphodiesterase IV than cyclic nucleotide phosphodiesterase types I, III, or V and have IC50 values ranging from 0.1 nM to 40 .mu.M for PDE activity. At concns. from 5x10-9M to 10-5M, preferably 5x10-9 to 10-7, compds. produced about 50% relaxation of guinea-pig tracheal strips. When administered at EDs of 4 to 1000 .mu.g/kg, preferably 4 to 50 .mu.g/kg, compds. produced 30% to 90% decrease in bronchospasm without any significant effect on blood pressure. At oral doses of 1 to 50 mg/kg, preferably 1 to 10 mg/kg, and inhaled doses of 4 to 1000 .mu.g/kg, preferably 4 to 50 .mu.g/kg, compds. inhibited by at least 50% ovalbumin-induced eosinophilia in guinea-pigs. Compds. produced 50% inhibition of LPS-induced TNF-.alpha. release from human PBMs at concns. of 10-9M to 10-6M, preferably 10-9M to 10-8 M. At doses of 1 to 1000 .mu.g/kg (i.t.), preferably 1 to 20 .mu.g/kg (i.t.), compds. inhibited antigen-induced bronchoconstriction by up to 80%. Compds. inhibited LPS-induced serum TNF-.alpha. at doses of 10 to 10,000 .mu.g/kg, preferably 10 to 250 .mu.g/kg. Compds. showed very low mammalian toxicity levels. Twenty-one compns. of the title compds. for gelatin capsules or dry powder inhalers were also prepd.

AN 1999:505666 CAPLUS

DN 131:144417

TI N-(Hetero)aryl-3,4-(cyclo)alkoxybenzamides and analogs useful as tumor necrosis factor and c-AMP phosphodiesterase inhibitors

IN Fenton, Garry; Morley, Andrew David; Palfreyman, Malcolm Norman; Ratcliffe, Andrew James; Harp, Brian William; Thurairatnam, Sukanthini; Vacher, Bernard Yvon Jack; Ashton, Michael John; Cook, David Charles; Hills, Susan Jacqueline; McFarlane, Ian Michael; Vicker, Nigel

PA Rhone-Poulenc Rorer Ltd., UK

SO U.S., 48 pp.
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 3

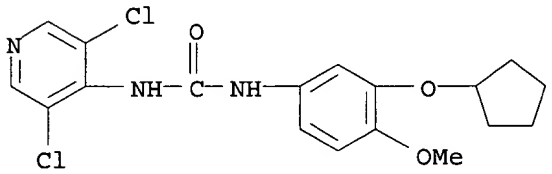
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5935978	A	19990810	US 1993-98178	19930728
	ZA 9200547	A	19930503	ZA 1992-547	19920127
	WO 9212961	A1	19920806	WO 1992-GB153	19920128
	W: AU, CA, CS, FI, HU, JP, KR, NO, PL, RU, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
	AU 9211881	A1	19920827	AU 1992-11881	19920128
	AU 664694	B2	19951130		
	EP 569414	A1	19931118	EP 1992-903462	19920128
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 06504782	T2	19940602	JP 1992-503280	19920128
	PL 169994	B1	19960930	PL 1992-300142	19920128
	CZ 281894	B6	19970312	CZ 1993-1528	19920128
	NO 9302701	A	19930921	NO 1993-2701	19930727
	ZA 9305448	A	19940519	ZA 1993-5448	19930728
	FI 9500375	A	19950127	FI 1995-375	19950127
	US 5679696	A	19971021	US 1995-484805	19950607
	US 5698711	A	19971216	US 1995-487377	19950607
	US 5840724	A	19981124	US 1997-881888	19970624
	US 6255326	B1	20010703	US 1999-239075	19990127
	US 6096768	A	20000801	US 1999-301877	19990429
PRAI	GB 1991-1777	A	19910128		
	GB 1991-17727	A	19910816		
	WO 1992-GB153	B2	19920128		
	GB 1992-15989	A	19920728		
	GB 1992-16005	A	19920728		
	GB 1992-16006	A	19920728		
	GB 1992-16008	A	19920728		
	GB 1992-16764	A	19920807		
	GB 1993-10633	A	19930521		
	GB 1993-10938	A	19930527		
	GB 1993-11281	A	19930601		
	GB 1993-14847	A	19930716		
	US 1993-98178	A3	19930728		
	US 1995-484805	A3	19950607		

OS MARPAT 131:144417

IT **159782-49-7P**, N-(3,5-Dichloropyrid-4-yl)-N'-(3-cyclopentyloxy-4-methoxyphenyl)urea
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(hetero)aryl 3,4-(cyclo)alkoxybenzamides and analogs useful as tumor necrosis factor and c-AMP phosphodiesterase inhibitors)

RN 159782-49-7 CAPLUS

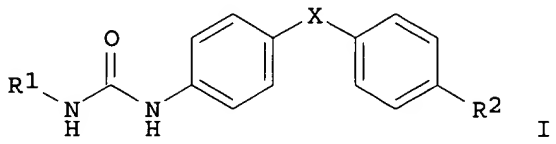
CN Urea, N-[3-(cyclopentyloxy)-4-methoxyphenyl]-N'-(3,5-dichloro-4-pyridinyl)- (9CI) (CA INDEX NAME)



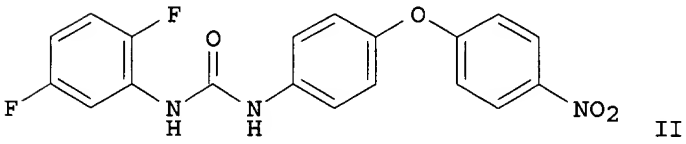
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI



I



II

AB The invention relates to 1,3-disubstituted ureas I [R1 = (un)substituted aryl; R2 = NO2, NH2; X = O, S], and a method of prepg. them by treating arom. amines with isocyanates. The isocyanates may be formed in situ, and the reaction carried out in a solvent such as toluene, at, e.g., 80.degree.C. If a nitro group is formed, it may be reduced with H2 in the presence of a Pd catalyst to give an amino group. The obtained 1,3-disubstituted ureas are inhibitors of the activity of the enzyme acyl co-enzyme A:cholesterol acyltransferase (ACAT), and may be used to inhibit cholesterol esterification and absorption in hypercholesterolemia. For instance, reaction of 4-(4'-nitrophenoxy)aniline with 2,5-difluorophenyl isocyanate gave 76% title compd. II. The latter gave 49% inhibition of rat liver ACAT at 2 .mu.M, and 58% inhibition of ACAT in rabbit intestinal mucosa, at the same concn., both in vitro.

AN 1999:421643 CAPLUS
DN 131:73441
TI 1,3-Disubstituted ureas useful as ACAT inhibitors, and method for their preparation
IN Oremus, Vladimir; Smahovsky, Vendelin; Faberova, Viera; Kakalik, Ivan; Schmidtova, Ludmila; Zemanek, Marian
PA Slovako- Farma, A.S., Slovakia
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9932437	A1	19990701	WO 1998-SK19	19981216

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	AU 9916976	A1	19990712	AU 1999-16976	19981216
	EP 1042278	A1	20001011	EP 1998-961715	19981216
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI, RO				
	JP 2001526259	T2	20011218	JP 2000-525374	19981216
	US 6444691	B1	20020903	US 2000-581821	20000710
PRAI	SK 1997-1751	A	19971219		
	WO 1998-SK19	W	19981216		

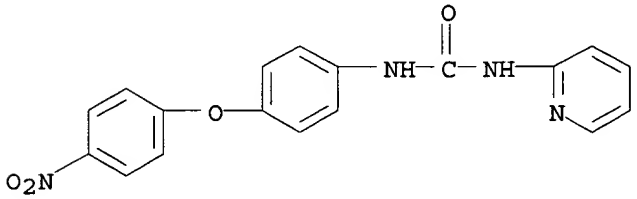
OS MARPAT 131:73441

IT **228544-41-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 1,3-disubstituted ureas as ACAT inhibitors)

RN 228544-41-0 CAPLUS

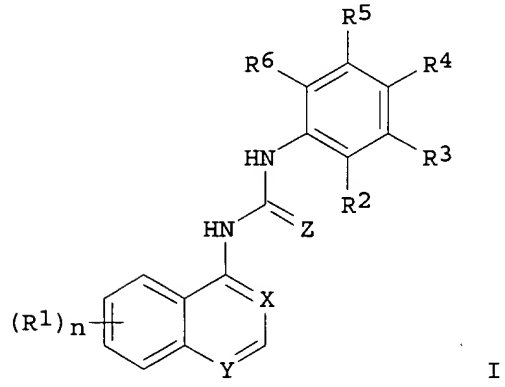
CN Urea, N-[4-(4-nitrophenoxy)phenyl]-N'-2-pyridinyl- (9CI) (CA INDEX NAME)



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 26 CAPLUS COPYRIGHT 2002 ACS

GI



I

AB Title compds. [I; X, Y = CH, N, provided that X and Y do not both = CH; Z = O, S; R1 = halo, R7CO, R8R9NCO, (substituted) alkyl, alkenyl, alkoxy; R2-R6 = H, halo, NO2, cyano, aryloxy, arylalkyloxy, arylalkyl, R7CO, R7SO2NH, R7CONR10, NR8R9, NR8R9CO, COR8, heterocyclyl, (substituted) alkyl, alkenyl, alkoxy, alkylthio, provided that .gtoreq.1 of R2-R6 is other than H; an adjacent pair of R2- R6 = atoms to form a (substituted)

carbocyclic or heterocyclic ring; R7 = alkyl, aryl; R8, R9 = H, alkyl, aryl, aralkyl; R10 = H, alkyl; n = 0-4], were prepd. Thus, quinoline-4-carbonyl azide (prepn. given) was refluxed 1 h in PhMe; 5-amino-1-methylindole in CH2Cl2 was added and the mixt. was stirred 16 h at room temp. to give 1-(1-methyl-1H-indol-5-yl)-3-quinolin-4-ylurea. The latter showed pKb >7 in an assay of human HFGAN72 antagonist activity.

AN 1999:139841 CAPLUS

DN 130:196581

TI Preparation of quinolinylureas and related compounds as HFGAN72 antagonists.

IN Chan, George; Johns, Amanda; Jurewicz, Anthony; Porter, Roderick Alan; Widdowson, Katherine

PA Smithkline Beecham Plc, UK

SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

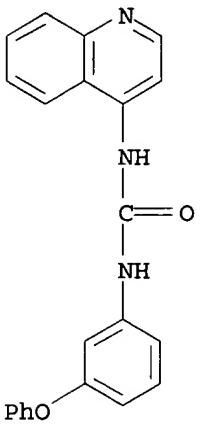
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9909024	A1	19990225	WO 1998-GB2437	19980813
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2300178	AA	19990225	CA 1998-2300178	19980813
	AU 9887411	A1	19990308	AU 1998-87411	19980813
	EP 1003737	A1	20000531	EP 1998-938812	19980813
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
	JP 2001515075	T2	20010918	JP 2000-509705	19980813
	US 6410529	B1	20020625	US 2000-485623	20000510
PRAI	GB 1997-17178	A	19970814		
	GB 1998-7756	A	19980408		
	WO 1998-GB2437	W	19980813		

OS MARPAT 130:196581

IT **220844-29-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinolinylureas and related compds. as HFGAN72 antagonists)

RN 220844-29-1 CAPLUS

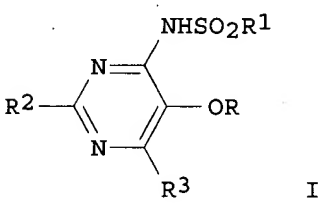
CN Urea, N-(3-phenoxyphenyl)-N'-4-quinolinyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI



I

AB Title compds. [I; R = (un)substituted Ph; R1 = heterocyclyl (sic); R2 = H, alkyl, alkoxy, Ph, etc.; R3 = CHO, (un)substituted alkyl, alkoxy, etc.] were prepd. Thus, 4,6-dichloro-5-(2-methoxyphenoxy)-2,2'-bipyrimidine was condensed with 5-tert-butylthiophene-2-sulfonamide K salt and the product etherified by (HOCH2)2 to give I [R = OC6H4(OMe)-2, R1 = 5-tert-butyl-2-thienyl, R2 = 2-pyrimidinyl, R3 = OCH2CH2OH]. Data for biol. activity of I were given.
AN 1998:749411 CAPLUS
DN 130:13993
TI Preparation of N-(phenoxypyrimidinyl)heteroaromatic sulfonamides as endothelin antagonists
IN Breu, Volker; Burri, Kaspar; Cassal, Jean-marie; Clozel, Martine; Hirth, Georges; Loffler, Bernd-michael; Muller, Marcel; Neidhart, Werner; Ramuz, Henri
PA Hoffmann-La Roche Inc., USA
SO U.S., 17 pp., Cont.-in-part of U. S. Ser. No. 676,313.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	US 5837708	A	19981117	US 1996-730422	19961015
	WO 9616963	A1	19960606	WO 1995-CH131	19950606
	W: CH, US				
	ZA 9509808	A	19960527	ZA 1995-9808	19951117
	BR 9505528	A	19971104	BR 1995-5528	19951127
PRAI	CH 1994-3559	A	19941125		
	WO 1995-CH131	A	19950606		
	US 1996-676313	A2	19960718		

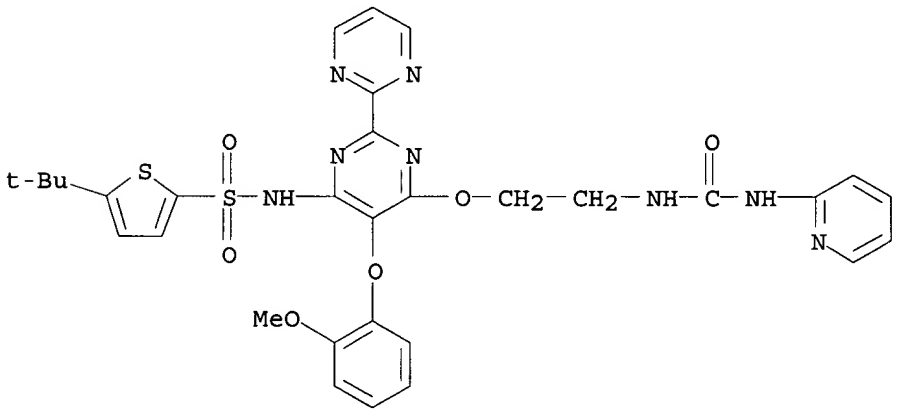
OS MARPAT 130:13993

IT **179400-23-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(phenoxypyrimidinyl)heteroarom. sulfonamides as endothelin antagonists)

RN 179400-23-8 CAPLUS

CN 2-Thiophenesulfonamide, 5-(1,1-dimethylethyl)-N-[5-(2-methoxyphenoxy)-6-[2-[[(2-pyridinylamino)carbonyl]amino]ethoxy][2,2'-bipyrimidin]-4-yl]- (9CI) (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 26 CAPLUS COPYRIGHT 2002 ACS

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

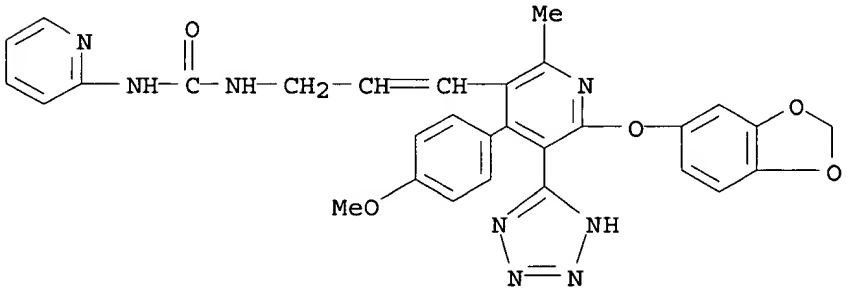
AB The title compds. (I; R1 - R11 = H, halo, OH, NH2, NO2, lower alkyl, alkoxy, alkenyl, alkylamino, alkylthio, alkanoyl, hydroxyalkyl, hydroxyalkoxy, hydroxyalkenyl, haloalkyl, haloalkoxy, or haloalkenyl, aryl-lower alkoxy, aroyl; or two of R1 - R5 groups or two of R7 - R11 groups are linked to each other to form a ring; R6 = an acidic functional group; R12 = aryl, heteroaryl, heterocyclylcarbonyl, or groups listed for R1 - R5 and R7 - R11; X = CR13R14, NR15, O, S; Y = NR16, O, S, CR17:CR18; R13 - R18 = H, lower alkyl; Z = H, OH, CO2H, lower alkoxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbamoyl, arylcarbamoyl,

heteroarylcarbamoyl, NH2, alkylamino, arylamino, heteroarylamino, acylamino, O2CNR19R20, NR21CONR22R23, O-CO2R24, NR25CO2R26, OR27, O2CR28; R19 - R28 = H, lower alkyl, aryl, heteroaryl; or R19 and R20, R21 and R22, R21 and R23, R22 and R23, or R25 and R26 are bonded to each other to form a ring; m = 0,1; n = 0-3) are prepd. They are useful for the treatment of hypertension, Raynaud's disease, acute kidney failure, myocardial infarction, angina pectoris, cerebral infarction, atrophy of brain blood vessels, arteriosclerosis, bronchial asthma, stomach ulcer, acute liver failure, diabetes, endotoxin shock, multi-organ failure, disseminated intravascular agglutination, and/or cyclosporin-induced kidney disorders. Thus, 3-cyano-5-(3-hydroxy-1-propenyl)-4-(4-methoxyphenyl)-6-methyl-2-(3,4-methylenedioxyphenyl)pyridine was dissolved in toluene, treated with Bu3SnN3, and refluxed overnight to give 60.5% the title 4-phenyl-3-tetrazolylpyridine compd. (II). II in vitro inhibited the binding of [125I]endotoxin to a pig ventricular muscle membrane prepn. with a -pIC50 value of 8.1.

AN 1998:81044 CAPLUS
DN 128:192655
TI Preparation of 4-phenylpyridine derivatives as endothelin antagonists
IN Sakurai, Kuniya; Niwa, Seiji; Oono, Seiji; Uchita, Hirohisa
PA Ajinomoto Co., Inc., Japan
SO Jpn. Kokai Tokkyo Koho, 95 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 10029979	A2	19980203	JP 1997-93782	19970411
PRAI JP 1996-91272		19960412		

OS MARPAT 128:192655
IT **203802-04-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of phenylpyridine derivs. as endothelin antagonists for treatment endothelin-related diseases)
RN 203802-04-4 CAPLUS
CN Urea, N-[3-[6-(1,3-benzodioxol-5-yloxy)-4-(4-methoxyphenyl)-2-methyl-5-(1H-tetrazol-5-yl)-3-pyridinyl]-2-propenyl]-N'-2-pyridinyl- (9CI) (CA INDEX NAME)



L4 ANSWER 15 OF 26 CAPLUS COPYRIGHT 2002 ACS
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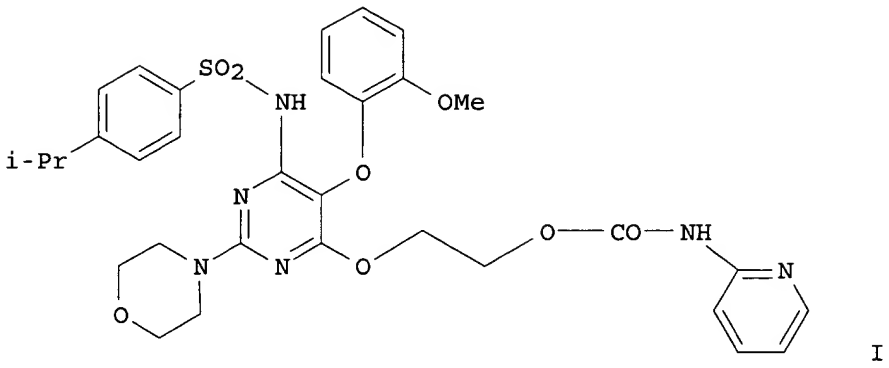


I

AB Implementation of a pyridylcarbamoyl group and an isopropylpyridylsulfonamide substituent as key components in the scaffold of Bosentan resulted in the identification of the potent orally active endothelin receptor antagonist Ro 48-5695 (I). It shows affinities for ETA and ETB receptors in the low nanomolar range and high functional antagonistic potency in vitro.

AN 1997:633849 CAPLUS

DN 127:307357

TI Discovery of RO 48-5695: a potent mixed endothelin receptor antagonist optimized from bosentan

AU Neidhart, Werner; Breu, Volker; Burri, Kaspar; Clozel, Martine; Hirth, Georges; Klinkhammer, Uwe; Giller, Thomas; Ramuz, Henri

CS Pharma Div., Preclinical Res., F. Hoffmann-La Roche Ltd., Basel, CH-4070, Switz.

SO Bioorganic & Medicinal Chemistry Letters (1997), 7(17), 2223-2228
CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier

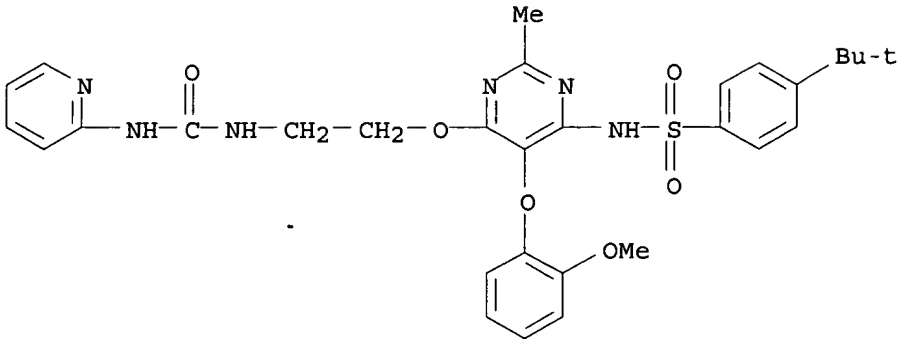
DT Journal

LA English

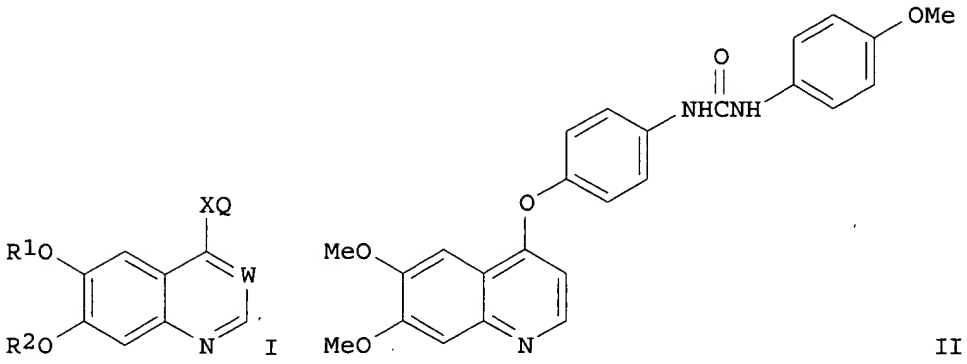
IT **167403-34-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of RO 48-5695, a potent mixed endothelin receptor antagonist optimized from bosentan)

RN 167403-34-1 CAPLUS

CN Benzenesulfonamide, 4-(1,1-dimethylethyl)-N-[5-(2-methoxyphenoxy)-2-methyl-6-[2-[[(2-pyridinylamino)carbonyl]amino]ethoxy]-4-pyrimidinyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 16 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI



AB The title compds. I [R1 and R2 represent each H or C1-4 alkyl, or R1 and R2 together form C1 to C3 alkylene; X represents O, S or CH2; W represents CH or N; and Q represents substituted aryl or substituted heteroaryl] are prepd. I inhibit platelet-derived growth factor receptor autophosphorylation and are useful in the treatment of cancer, arthritis, etc. The title compd. II (prepn. given) (at 100 mg/kg i.p. once daily for 9 days) increased the survival of mice with transplanted leukemic P388 cells by 130%.

AN 1997:414195 CAPLUS

DN 127:34137

TI Preparation of quinoline and quinazoline derivatives inhibiting platelet-derived growth factor receptor autophosphorylation

IN Kubo, Kazuo; Ohyama, Shinichi; Shimizu, Toshiyuki; Nishitoba, Tsuyoshi; Kato, Shinichiro; Murooka, Hideko; Kobayashi, Yoshiko; et al.

PA Kirin Beer Kabushiki Kaisha, Japan; Kubo, Kazuo; Ohyama, Shinichi; Shimizu, Toshiyuki; Nishitoba, Tsuyoshi; Kato, Shinichiro

SO PCT Int. Appl., 243 pp.
CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 9717329	A1	19970515	WO 1996-JP3229	19961105
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9673400	A1	19970529	AU 1996-73400	19961105
	EP 860433	A1	19980826	EP 1996-935541	19961105
	EP 860433	B1	20020703		
	R: CH, DE, FR, GB, LI				
	US 6143764	A	20001107	US 1998-68660	19980506
PRAI	JP 1995-313555	A	19951107		
	JP 1996-62121	A	19960223		
	WO 1996-JP3229	W	19961105		

OS MARPAT 127:34137

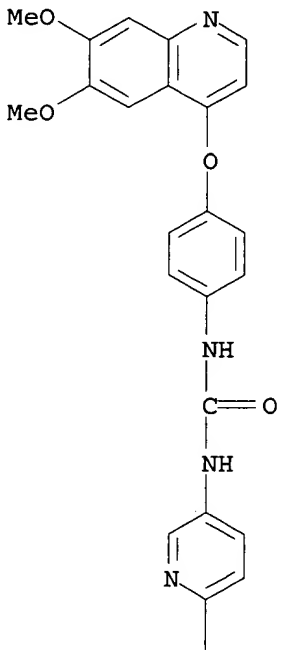
IT **190727-92-5P**

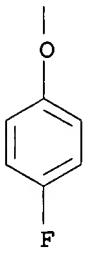
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinoline and quinazoline derivs. inhibiting platelet-derived growth factor receptor autophosphorylation)

RN 190727-92-5 CAPLUS

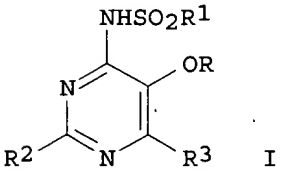
CN Urea, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-[6-(4-fluorophenoxy)-3-pyridinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A





L4 ANSWER 17 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI



I

AB Title compds. [I; R = (un)substituted Ph; R1 = heterocyclyl; R2 = H, alkyl, alkoxy, Ph, heterocyclyl, etc.; R3 = alkyl, alkoxy, CHO, etc.] were prepd. Thus, 5-tert-butyl-2-thiophenesulfonamide was N-arylated by 4,6-dichloro-5-(2-methoxyphenoxy)-2,2'-bipyrimidine and the product etherified by HOCH2CH2OH to give I [R = 1g(OMe)-2, R1 = 5-tert-butyl-2-thienyl, R2 = 2-pyrimidinyl, R3 = OCH2CH2OH]. Data for inhibition of endothelin-induced rat aorta contraction by 2 prepd. I were given.

AN 1996:469485 CAPLUS

DN 125:114678

TI Preparation of N-(4-pyrimidinyl)sulfonamides as endothelin receptor antagonists

IN Breu, Volker; Burri, Kaspar; Cassal, Jean-Marie; Clozel, Martine; Hirth, Georges; Loeffler, Bernd-Michael; Mueller, Marcel; Neidhart, Werner; Ramuz, Henri

PA F. Hoffmann-La Roche Ag, Switz.

SO Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW

DT Patent

LA German

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 713875	A1	19960529	EP 1995-117833	19951113
	EP 713875	B1	20010321		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CA 2162630	AA	19960526	CA 1995-2162630	19951110
	AT 199905	E	20010415	AT 1995-117833	19951113
	ES 2156179	T3	20010616	ES 1995-117833	19951113
	AU 9537895	A1	19960530	AU 1995-37895	19951116
	AU 691353	B2	19980514		
	ZA 9509808	A	19960527	ZA 1995-9808	19951117

	JP 08208625	A2	19960813	JP 1995-300933	19951120
	JP 2755565	B2	19980520		
	HU 75030	A2	19970328	HU 1995-3311	19951120
	IL 116064	A1	20000629	IL 1995-116064	19951120
	NO 9504718	A	19960528	NO 1995-4718	19951122
	CZ 289920	B6	20020417	CZ 1995-3088	19951123
	FI 9505669	A	19960526	FI 1995-5669	19951124
	CN 1132751	A	19961009	CN 1995-120250	19951124
	CN 1064965	B	20010425		
	TW 394763	B	20000621	TW 1995-84112546	19951124
	RU 2162084	C2	20010120	RU 1995-120013	19951124
	BR 9505528	A	19971104	BR 1995-5528	19951127
PRAI	CH 1994-3559	A	19941125		
	CH 1995-2842	A	19951009		

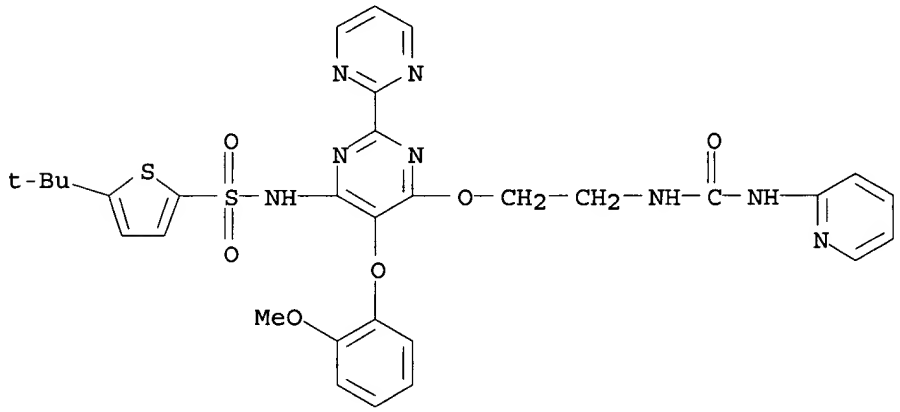
OS MARPAT 125:114678

IT **179400-23-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(4-pyrimidinyl)sulfonamides as endothelin receptor antagonists)

RN 179400-23-8 CAPLUS

CN 2-Thiophenesulfonamide, 5-(1,1-dimethylethyl)-N-[5-(2-methoxyphenoxy)-6-[2-[[(2-pyridinylamino)carbonyl]amino]ethoxy][2,2'-bipyrimidin]-4-yl]- (9CI) (CA INDEX NAME)



L4 ANSWER 18 OF 26 CAPLUS COPYRIGHT 2002 ACS

AB R4YC6H4(CH2)nNR2CONHR3 [R2 = (ar)alkyl, heterocyclyl(alkyl), alkoxyalkyl, etc.; R3,R4 = (un)substituted aryl, heterocyclyl; Y = bond, alkylene, O, CO, CONH, etc.; n = 0 or 1] were prep. Thus, 1-cycloheptyl-1-(4-phenoxyphenylmethyl)-3-(2,4,6-trifluorophenyl)urea had IC50 of 1.1x10-8M against cholesterol acyltransferase in vitro.

AN 1996:455768 CAPLUS

DN 125:114322

TI Preparation of urea derivatives as cholesterol acyltransferase inhibitors

IN Terasawa, Takeshi; Tanaka, Akira; Chiba, Toshiyuki; Takasugi, Hisashi

PA Fujisawa Pharmaceutical Co., Ltd., Japan

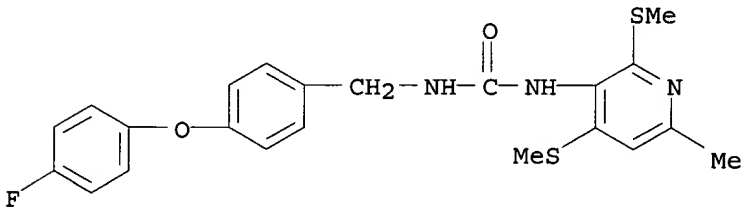
SO PCT Int. Appl., 228 pp.
CODEN: PIXXD2

DT Patent

LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9610559	A1	19960411	WO 1995-JP1982	19950929
	W: AU, CA, CN, HU, JP, KR, MX, RU, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2200981	AA	19960411	CA 1995-2200981	19950929
	AU 9535779	A1	19960426	AU 1995-35779	19950929
	EP 784612	A1	19970723	EP 1995-932934	19950929
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 10510512	T2	19981013	JP 1995-511616	19950929
	ZA 9508365	A	19960508	ZA 1995-8365	19951004
PRAI	GB 1994-19970		19941004		
	GB 1995-6720		19950331		
	GB 1995-14021		19950710		
	WO 1995-JP1982		19950929		

OS MARPAT 125:114322
IT **179057-08-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of urea derivs. as cholesterol acyltransferase inhibitors)
RN 179057-08-0 CAPLUS
CN Urea, N-[[4-(4-fluorophenoxy)phenyl]methyl]-N'-[6-methyl-2,4-bis(methylthio)-3-pyridinyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 19 OF 26 CAPLUS COPYRIGHT 2002 ACS
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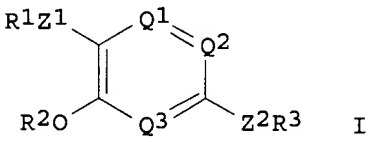


I

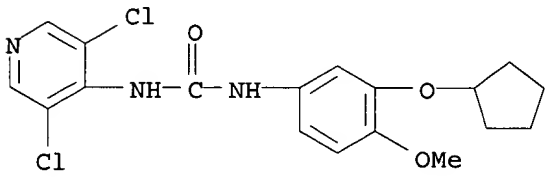
AB The title compds. [I; Q1-Q3 = N, CX, CH; X = halogen; R1 = (un)substituted lower alkyl group; R2 = (un)substituted oxaaliph.; R3 = (un)substituted aryl or heteroaryl; Z1 = O, S; Z2 = CH:CH, C.tplbond.C, CH2CZ, CZCH2, CZCZ, CH2NH, CH2O, CH2S, CX2O, CZNH, NHCH2, OCH2, SCH2, SOCH2, SO2CH2, OCX2, OCZ, NHCZ, N:N, NHSO2, SO2NH, SO2NH, CZCZNH, NHCOO, OCONH, NHCONH; Z = O, S] [e.g., N-(3,5-dichloro-1-oxido-4-pyridino)-4-difluoromethoxy-3-(tetrahydro-3-furyloxy)benzamide, m.p. 169-171.degree. (decompn.)], useful for inhibiting the prodn. or physiol. effects of tumor necrosis factor and inhibiting cyclic-AMP phosphodiesterase, are prepd. and I-contg.

formulations presented. I demonstrate phosphodiesterase IC50 values of 0.1 nM to 40 .mu.M.

AN 1995:994180 CAPLUS
DN 124:55798
TI Preparation of substituted (hetero)aromatic compounds as cyclic-AMP phosphodiesterase and TNF inhibitors
IN Fenton, Garry; Palfreyman, Malcolm Norman; Thurairatnam, Sukanthini
PA Rhone-Poulenc Rorer Ltd., UK
SO PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9520578	A1	19950803	WO 1995-GB157	19950126
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US				
	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9514631	A1	19950815	AU 1995-14631	19950126
	ZA 9500639	A	19960726	ZA 1995-639	19950126
	EP 741707	A1	19961113	EP 1995-906437	19950126
	EP 741707	B1	19980401		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09509654	T2	19970930	JP 1995-519939	19950126
	AT 164575	E	19980415	AT 1995-906437	19950126
PRAI	GB 1994-1460		19940126		
	WO 1995-GB157		19950126		

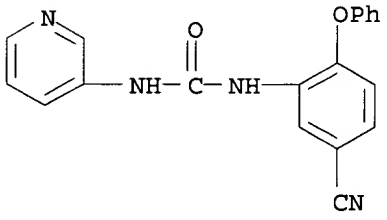
OS MARPAT 124:55798
IT **159782-49-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted (hetero)arom. compds. as cyclic-AMP phosphodiesterase and TNF inhibitors)
RN 159782-49-7 CAPLUS
CN Urea, N-[3-(cyclopentyloxy)-4-methoxyphenyl]-N'-(3,5-dichloro-4-pyridinyl)- (9CI) (CA INDEX NAME)



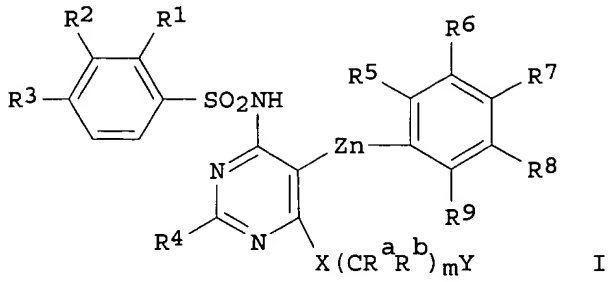
L4 ANSWER 20 OF 26 CAPLUS COPYRIGHT 2002 ACS
AB The results of the efforts aimed at the replacement of the benzopyran ring of the lead cardiac selective antiischemic ATP-sensitive potassium channel (KATP) opener (I) are described. Systematic modification of the benzopyran ring of I resulted in the discovery of a structurally simpler acyclic analog (II) with slightly lower antiischemic potency than I.

Further structure-activity studies on the acyclic analog II provided the 2-phenoxy-3-pyridylurea analog (III) with improved antiischemic potency and selectivity compared to the benzopyran-based I. These data demonstrate that the benzopyran ring of I and its congeners is not mandatory for antiischemic activity and cardiac selectivity. The results described also show that, as for the benzopyran class of compds., the structure-activity relations for the antiischemic and vasorelaxant activities of KATP openers are distinct. The mechanism of action of the acyclic analogs (e.g., III) still appears to involve KATP opening as their cardioprotective effects are abolished by pretreatment with the KATP blocker glyburide.

AN 1995:983072 CAPLUS
DN 124:75535
TI Cardioselective Antiischemic ATP-Sensitive Potassium Channel Openers. 4. Structure-Activity Studies on Benzopyranylcyanoguanidines: Replacement of the Benzopyran Portion
AU Atwal, Karnail S.; Ferrara, Francis N.; Ding, Charles Z.; Grover, Gary J.; Sleph, Paul G.; Dzwonczyk, Steven; Baird, Anne J.; Normandin, Diane E.
CS Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, NEW JERSEY, USA
SO Journal of Medicinal Chemistry (1996), 39(1), 304-13
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
IT **166263-16-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(structure-activity studies of potassium channel opener benzopyranylcyanoguanidines)
RN 166263-16-7 CAPLUS
CN Urea, N-(5-cyano-2-phenoxyphenyl)-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



L4 ANSWER 21 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI



I

AB Title compds. (I; R1-R3 = H, alkyl, alkoxy, alkylthio, alkenyl, halo, CF3, hydroxyalkoxy, haloalkoxy, alkanoylalkyl, hydroxyalkyl, CO2H, amino, etc.; R2R3, R5R6, R6R7 = butadienyl, methylenedioxy, ethylenedioxy, isopropylidenedioxy; R4 = H, alkyl, cycloalkyl, CF3, alkoxy, alkynyloxy, alkylthio, alkylthioalkyl, hydroxyalkyl, dihydroxyalkoxy, alkylsulfinyl, alkylsulfonyl, aryl, arylthio, aryloxy, heterocyclyl, heterocyclylalkyl, etc.; R5-R9 = H, halo, CF3, alkyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl; Ra, Rb = H, alkyl, alkoxy, alkylthio; X = O, S, NH; Y = O2CNR10R11, HNOCNR10R11, O2COR10, HNCO2R10; R10 = alkyl, cycloalkyl, hydroxyalkyl, carboxyalkyl, alkoxycarbonylalkyl, alkanoyloxyalkyl, arylcarbamoylalkyl, heterocyclyl, heterocyclylalkyl, etc.; R11 = H, R10; m = 1-3; n = 0,1), were prepd. Thus, 2-pyridinecarbonyl azide was heated in PhMe; 4-tert-butyl-N-[6-(2-hydroxyethoxy)-5-(2-methoxyphenoxy)-2,2'-bipyrimidin-4-yl]benzenesulfonamide was added to give pyridine-2-carbaminic acid, 2-[6-(4-tert-butylphenylsulfonylamino)-5-(2-methoxyphenoxy)-2,2'-bipyrimidin-4-yloxy]ethyl ester. The latter at 30 mg/kg orally in rats gave a 30% redn. in av. arterial blood pressure.

AN 1995:780258 CAPLUS

DN 123:169647

TI Preparation of sulfonylaminopyrimidines as endothelin antagonists.

IN Breu, Volker; Burri, Kaspar; Cassal, Hean-Marie; Clozel, Martine; Hirth, Georges; Loeffler, Bernd-Michael; Mueller, Marcel; Neidhart, Werner; Ramuz, Henri

PA F. Hoffmann-La Roche AG, Switz.

SO Eur. Pat. Appl., 46 pp.
CODEN: EPXXDW

DT Patent

LA German

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 633259	A1	19950111	EP 1994-109257	19940616
	EP 633259	B1	19990113		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	TW 394761	B	20000621	TW 1994-83105221	19940608
	CA 2125730	AA	19941229	CA 1994-2125730	19940613
	AT 175669	E	19990115	AT 1994-109257	19940616
	ES 2127850	T3	19990501	ES 1994-109257	19940616
	ZA 9404434	A	19950103	ZA 1994-4434	19940621
	IL 110089	A1	20000831	IL 1994-110089	19940622
	AU 9465948	A1	19950105	AU 1994-65948	19940624
	AU 678467	B2	19970529		
	HU 67636	A2	19950428	HU 1994-1907	19940624
	FI 9403084	A	19941229	FI 1994-3084	19940627
	NO 9402428	A	19941229	NO 1994-2428	19940627
	BR 9402558	A	19950328	BR 1994-2558	19940627

	CN 1106007	A	19950802	CN 1994-106574	19940627
	CN 1050839	B	20000329		
	LT 3723	B	19960226	LT 1994-1979	19940627
	LV 11175	B	19960620	LV 1994-131	19940627
	US 5541186	A	19960730	US 1994-266072	19940627
	PL 175771	B1	19990226	PL 1994-304007	19940627
	PL 177031	B1	19990930	PL 1994-323036	19940627
	RU 2142457	C1	19991210	RU 1994-22258	19940627
	CZ 287184	B6	20001011	CZ 1994-1573	19940627
	JP 07017972	A2	19950120	JP 1994-146003	19940628
	JP 2545200	B2	19961016		
	RO 114325	B3	19990330	RO 1994-1112	19940628
	SK 280736	B6	20000711	SK 1994-779	19940628
PRAI	CH 1993-1924	A	19930628		
	IL 1992-101650	A0	19920420		
	CH 1994-1575	A	19940520		

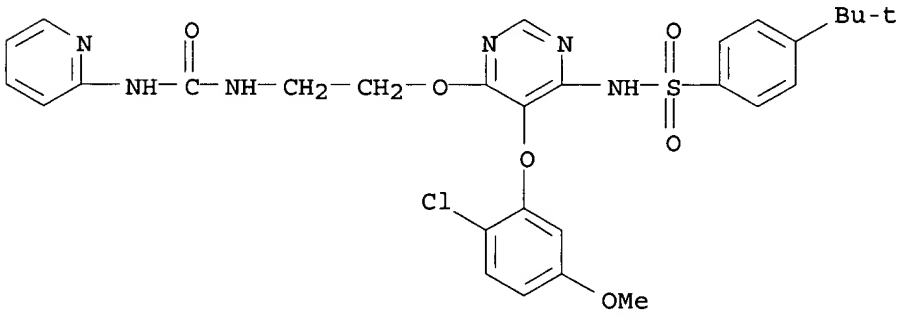
OS MARPAT 123:169647

IT **167403-30-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of sulfonylaminopyrimidines as endothelin antagonists)

RN 167403-30-7 CAPLUS

CN Benzenesulfonamide, N-[5-(2-chloro-5-methoxyphenoxy)-6-[2-[[(2-pyridinylamino)carbonyl]amino]ethoxy]-4-pyrimidinyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 22 OF 26 CAPLUS COPYRIGHT 2002 ACS

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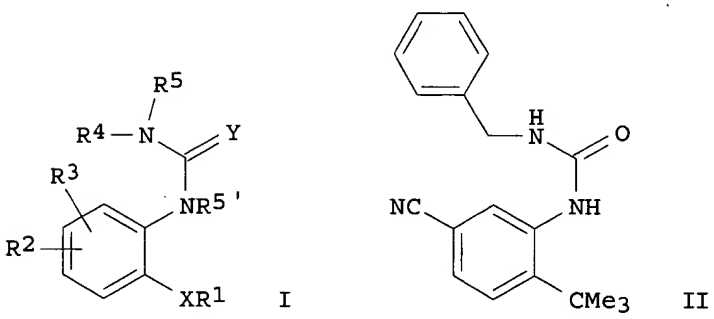

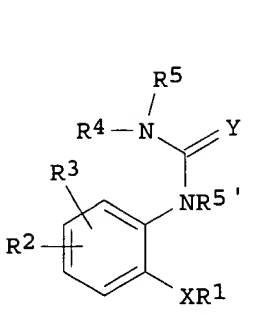

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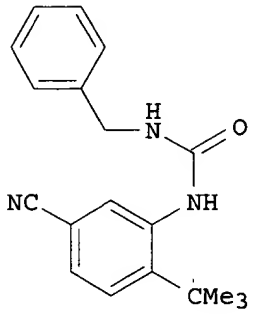


II

AB Title compds. I [X = single bond, O, CO, S, NH, or alkylimino; Y = O, S, or NCN; R1 = alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl; R2 = H, alkyl, haloalkyl, alkenyl, alkynyl, cyano, NO2, CHO, CO2H, halo, (un)substituted amino, etc.; R3 = H, alkyl, OH, alkoxy, (un)substituted amino, cyano, NO2; R4 = aryl, aralkyl, heterocyclo, heterocycloalkyl; R5, R5' = H, alkyl, (un)substituted alkylamino, haloalkyl; or R4R5 form ring with 5 to 7 members and optional O, S, or (un)substituted NH] and salts are claimed, along with 18 specific compds. which were also prepd. These compds. have potassium channel activating activity and are useful, e.g., as cardiovascular agents (no data). For example, tert-butylbenzene underwent 2,4-dinitration (70%), redn. of the 4-nitro group to amino (86%), diazotization and cyanation of the group to give a benzonitrile (42%), and redn. of the remaining nitro group with SnCl2 (100%) to give 3-amino-4-(tert-butyl)benzonitrile. Reaction of this with benzyl isocyanate gave title compd. II in 70% yield.

AN 1995:733459 CAPLUS

DN 123:143653

TI Biaryl ureas and related compounds for use as cardiovascular agents.

IN Atwal, Karnail; Ferrara, Francis N.; Ding, Charles Z.

PA USA

SO Can. Pat. Appl., 39 pp.
CODEN: CPXXEB

DT Patent

LA English

FAN.CNT 1

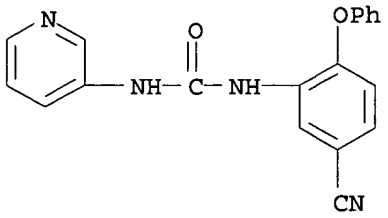
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CA 2132771	AA	19950408	CA 1994-2132771	19940923
	US 5547966	A	19960820	US 1993-134195	19931007
	EP 656350	A1	19950607	EP 1994-306813	19940916
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	AU 9474463	A1	19950427	AU 1994-74463	19941006
	AU 690133	B2	19980423		
	JP 07188151	A2	19950725	JP 1994-243895	19941007
PRAI	US 1993-134195		19931007		

OS MARPAT 123:143653

IT **166263-16-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biaryl ureas and analogs as cardiovascular agents)

RN 166263-16-7 CAPLUS

CN Urea, N-(5-cyano-2-phenoxyphenyl)-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



L4 ANSWER 23 OF 26 CAPLUS COPYRIGHT 2002 ACS
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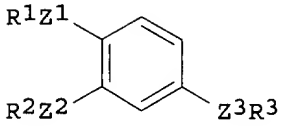

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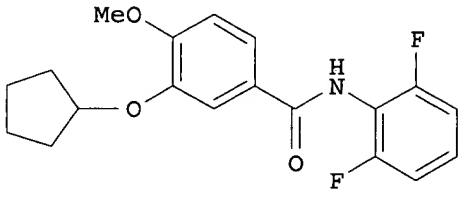

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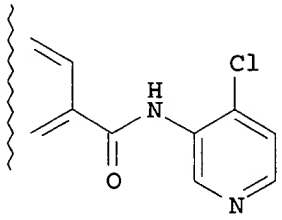


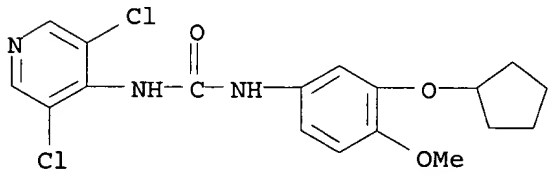
III

AB Title compds. I [R1 = alkyl; R2 = alkyl, alkenyl, cycloalkyl, cycloalkenyl, cyclothioalkyl, cyclothioalkenyl; R3 = aryl, heteroaryl; Z, Z1, Z2 = O, S; Z3 = CH:CH, C.tplbond.C, CH2C(:Z), C(:Z)CH2, C(:Z)C(:Z), C(:Z)NH, NHC(:Z), CH2NH, CH2O, CH2S, CX2O, N:N, NHSO2, NHCO2, etc.; X = halo] and their N-oxides and salts, for manuf. of medicaments for treatment of a wide variety of disease states modulated by tumor necrosis factor (TNF) inhibitors, are claimed. The invention also includes pharmaceutical use of I for inhibiting cAMP phosphodiesterases (PDE). For example, amidation of either 2,6-difluoroaniline or 4-chloropyrid-3-ylamine with 3-cyclopentyloxy-4-methoxybenzoyl chloride gave title compds. II and III, resp. I had IC50 of 10-9 to 10-5M for inhibition of porcine PDE IV, and were 50- to 10,000-fold more selective for cAMP PDE type IV than for types I, III, or V. I also inhibited eosinophil superoxide generation, showed bronchodilator activity in several tests, and inhibited LPS-induced serum TNF-.alpha. in mice. Examples include 77 prepns. of I, 111 ref. prepns. of precursors, and 21 pharmaceutical formulations.
AN 1995:257708 CAPLUS
DN 122:290715
TI N-Phenyl- and N-pyridylbenzamides and analogs useful as inhibitors of c-AMP phosphodiesterase and TNF
IN Fenton, Garry; Morley, Andrew David; Palfreyman, Malcolm Norman; Ratcliffe, Andrew James; Sharp, Brian William; Stuttle, Keith Alfred

James; Thurairatnam, Sukanthini; Vacher, Bernard Yvon Jack
PA Rhone-Poulenc Rorer Ltd., UK
SO PCT Int. Appl., 162 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9402465	A1	19940203	WO 1993-GB1597	19930728
	W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	ZA 9305448	A	19940519	ZA 1993-5448	19930728
	EP 652868	A1	19950517	EP 1993-917937	19930728
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 08503925	T2	19960430	JP 1993-504330	19930728
	HU 72656	A2	19960528	HU 1995-265	19930728
	FI 9500375	A	19950127	FI 1995-375	19950127
	NO 9500319	A	19950327	NO 1995-319	19950127
PRAI	GB 1992-15989	A	19920728		
	GB 1992-16005	A	19920728		
	GB 1992-16006	A	19920728		
	GB 1992-16008	A	19920728		
	GB 1992-16764	A	19920807		
	GB 1993-10633	A	19930521		
	GB 1993-10938	A	19930527		
	GB 1993-11281	A	19930601		
	GB 1993-14847	A	19930716		
	WO 1993-GB1597	W	19930728		

OS MARPAT 122:290715
IT **159782-49-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as inhibitor of c-AMP phosphodiesterase or TNF)
RN 159782-49-7 CAPLUS
CN Urea, N-[3-(cyclopentyloxy)-4-methoxyphenyl]-N'-(3,5-dichloro-4-pyridinyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 24 OF 26 CAPLUS COPYRIGHT 2002 ACS
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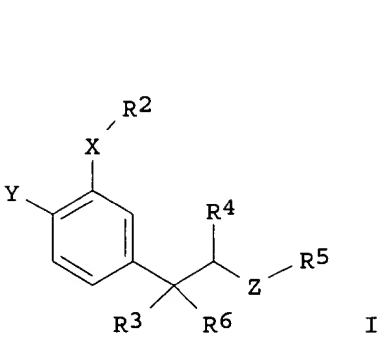

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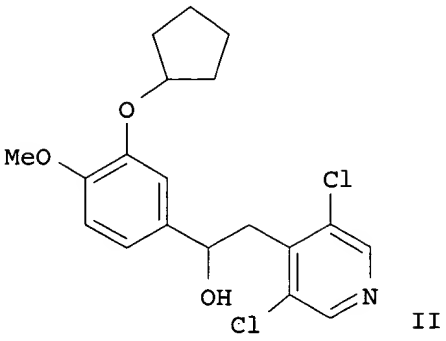


II

AB Title compds. I [wherein Y = halo or OR1; R1 = (un)substituted alkyl; X = O, S, or NR7, R7 = H, alkyl; R2 = (un)substituted cycloalkyl or cycloalkenyl; R3, R4 = H, alkyl, CO2R8 (where R8 = H, alkyl, aryl, or aralkyl), CONR9R10 (where R9, R10 = H, alkyl, aryl or aralkyl), CSNR9R10, cyano, CH2CN; Z = (CH2)n (where n = 0-3); R5 = (un)substituted mono- or bicyclic aryl group optionally contg. .gtoreq. 1 heteroatom(s) selected from O, S, or N; R6 = H or OH] and the salts, solvates, hydrates, prodrugs and N-oxides thereof are disclosed. The compds. are potent and selective inhibitors of phosphodiesterase (PDE) type IV, and are useful in the prophylaxis and treatment of diseases such as asthma, where unwanted inflammatory responses or muscular spasms are present. For example, lithiation of 3,5-dichloro-4-methylpyridine with LDA in THF at -70.degree., followed by reaction with 3-cyclopentyloxy-4-methoxybenzaldehyde, gave title compd. (.+-.)-II. I are said to show concn.-dependent inhibition of recombinant PDE IV at 0.1-1000 nM with little or no activity against PDE I, II, III, or V at up to 100 .mu.M. Prepns. of approx. 20 I and 20 intermediates, along with general ranges of results for addnl. biol. tests, are described.

AN 1995:207617 CAPLUS

DN 122:10065

TI Trisubstituted phenyl derivatives as phosphodiesterase inhibitors and processes for their preparation

IN Warrellow, Graham John; Cole, Valerie Anne; Alexander, Rikki Peter

PA Celltech Limited, UK

SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9420446	A1	19940915	WO 1994-GB453	19940309
	W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, UA, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2135480	AA	19940915	CA 1994-2135480	19940309
	AU 9461489	A1	19940926	AU 1994-61489	19940309
	AU 675511	B2	19970206		
	EP 640065	A1	19950301	EP 1994-908454	19940309
	EP 640065	B1	20011017		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 08505158	T2	19960604	JP 1994-519748	19940309

	AT 207051	E	20011115	AT 1994-908454	19940309
	ES 2162623	T3	20020101	ES 1994-908454	19940309
	US 5739144	A	19980414	US 1995-543962	19951017
	US 5962483	A	19991005	US 1998-8173	19980116
PRAI	GB 1993-4920	A	19930310		
	US 1994-208656	B1	19940309		
	WO 1994-GB453	W	19940309		
	US 1995-384612	B1	19950202		
	US 1995-543962	A3	19951017		

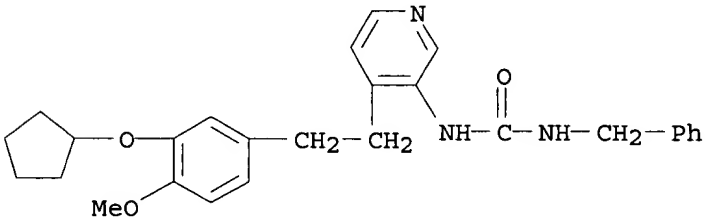
OS MARPAT 122:10065

IT **159196-19-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocyclic trisubstituted Ph derivs. as phosphodiesterase inhibitors)

RN 159196-19-7 CAPLUS

CN Urea, N-[4-[2-[3-(cyclopentyloxy)-4-methoxyphenyl]ethyl]-3-pyridinyl]-N'-(phenylmethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 25 OF 26 CAPLUS COPYRIGHT 2002 ACS

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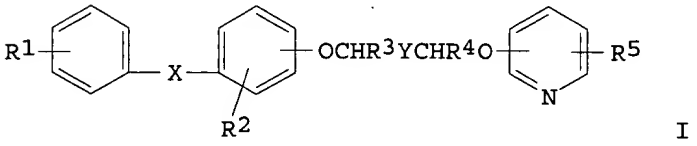


I

AB The title compds. I (R1 = H, halogen, alkyl, alkoxy, or haloalkyl; R2 = H, halogen, alkyl, alkenyl, haloalkyl, alkoxy, alkylthio, haloalkoxy, haloalkylthio; R3, R4 = H, alkyl, haloalkyl, alkoxyalkyl, alkenoxyalkyl, alkenyl, alkynyl, or together form a direct bond; R5 = H, halogen, alkyl, haloalkyl, alkoxy, NH2, alkyl, alkylamino, dialkylamino, or acylamino), as well as their salts, are prepd. for use as insecticides, esp. against fleas. Thus, Ph 4-[2-[2-(2-pyridyloxy)ethoxy)]ethoxy]phenyl ether (II) was prepd. by treating 2-[2-(4-phenoxyphenoxy)ethoxy]ethanol with 2-chloropyridine. II showed 100% activity against fleas both in vivo and in vitro tests.

AN 1990:458954 CAPLUS

DN 113:58954

TI Preparation of substituted pyridines as insecticides

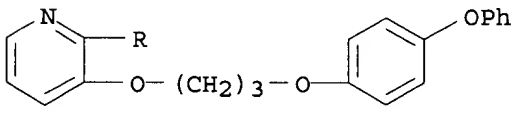
IN Alig, Bernd; Stendel, Wilhelm; Londershausen, Michael

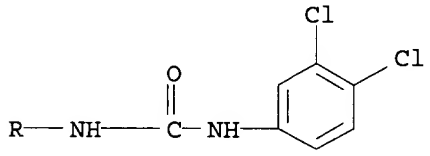
PA Bayer A.-G., Fed. Rep. Ger.

SO Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

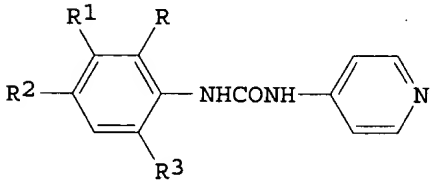
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 356797	A2	19900307	EP 1989-114980	19890812
EP 356797	A3	19910403		
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL				
DE 3828820	A1	19900322	DE 1988-3828820	19880825
JP 02117660	A2	19900502	JP 1989-215127	19890823
DK 8904186	A	19900226	DK 1989-4186	19890824
AU 8940252	A1	19900405	AU 1989-40252	19890824
AU 617513	B2	19911128		
BR 8904250	A	19900410	BR 1989-4250	19890824
ZA 8906454	A	19900530	ZA 1989-6454	19890824
PRAI DE 1988-3828820		19880825		

OS MARPAT 113:58954
IT **128262-28-2P**
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as insecticide)
RN 128262-28-2 CAPLUS
CN Urea, N-(3,4-dichlorophenyl)-N'-[3-[3-(4-phenoxyphenoxy)propoxy]-2-pyridinyl]- (9CI) (CA INDEX NAME)





L4 ANSWER 26 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI

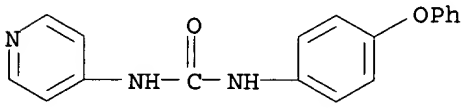


I

AB A series of N-phenyl-N'-pyridinylureas, e.g., I (R, R1, R2, R3 = H, Cl,

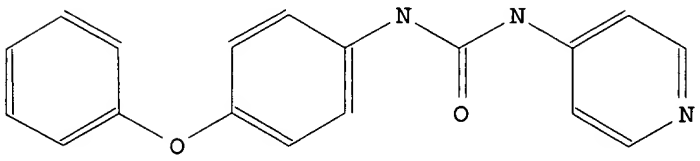
Br, F, CF3, Me, Et, CHMe2, NO2, NH2, OMe, etc.) was prepd. by the reaction of aryl isocyanates with 2-, 3-, of 4-aminopyridine. They were examd. for anticonvulsant activity. Extensive structure/activity investigations revealed optimal activity in the N-(2,6-disubstituted-phenyl)-N'-(4-pyridinyl)urea series, with I (R = Cl, R1 = R2 = H, R3 = Me) (II) exhibiting the best overall anticonvulsant profile. II was effective against seizures induced by maximal electroshock but did not protect mice from clonic seizures produced by the convulsant pentylenetetrazol. The overall pharmacol. profile suggests that II would be of therapeutic use in the treatment of generalized tonic-clonic and partial seizures. II was selected for Phase 1 clin. trials.

AN 1990:55554 CAPLUS
DN 112:55554
TI N-Phenyl-N'-pyridinylureas as anticonvulsant agents
AU Pavia, Michael R.; Lobbestael, Sandra J.; Taylor, Charles P.; Hershenson, Fred M.; Miskell, David L.
CS Parke-Davis Pharm. Res. Div., Warner-Lambert Co., Ann Arbor, MI, 48105, USA
SO J. Med. Chem. (1990), 33(2), 845-61
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
OS CASREACT 112:55554
IT **124420-93-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and anticonvulsant activity of)
RN 124420-93-5 CAPLUS
CN Urea, N-(4-phenoxyphenyl)-N'-4-pyridinyl- (9CI) (CA INDEX NAME)



L8 ANSWER 1 OF 1 BEILSTEIN COPYRIGHT 2002 BEILSTEIN CDS MDL

Beilstein Records (BRN):	3560216
Beilstein Pref. RN (BPR):	124420-93-5
CAS Reg. No. (RN):	**124420-93-5**
Chemical Name (CN):	1-(4-phenoxy-phenyl)-3-pyridin-4-yl-urea
Autonom Name (AUN):	1-(4-phenoxy-phenyl)-3-pyridin-4-yl-urea
Molec. Formula (MF):	C18 H15 N3 O2
Molecular Weight (MW):	305.34
Lawson Number (LN):	27378, 14892, 5219, 1762
Compound Type (CTYPE):	heterocyclic
Constitution ID (CONSID):	3152373
Tautomer ID (TAUTID):	3387514
Beilstein Citation (BSO):	6-22
Entry Date (DED):	1991/10/23
Update Date (DUPD):	1993/03/20



Field Availability:

Code	Name	Occurrence
BRN	Beilstein Records	1
BPR	Beilstein Preferred RN	1
RN	CAS Registry Number	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	4
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
BSO	Beilstein Citation	1
ED	Entry Date	1
UPD	Update Date	1
MP	Melting Point	1

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

Melting Point:

Value (MP) (Cel)	Solvent (.SOL)	Ref.
164 - 166	aq. ethanol	1

Reference(s):

1. Pavia, Michael R.; Lobbestael, Sandra J.; Taylor, Charles P.; Hershenson, Fred M.; Miskell, David L., J.Med.Chem., CODEN: JMCMAR, 33(2), <1990>, 854-861; BABS-5500188

Reaction:
RX

Reaction ID:	1529274
Reactant BRN:	393196, 105782
Reactant:	4-phenoxy-phenyl isocyanate, pyridin-4-ylamine
Product BRN:	3560216
Product:	1-(4-phenoxy-phenyl)-3-pyridin-4-yl-urea
No. of Reaction Details:	1

Reaction Details:
RX

Reaction RID:	1529274.1
Reaction Classification:	Preparation
Yield:	66 percent (BRN=3560216)
Solvent:	tetrahydrofuran

Reference(s):

1. Pavia, Michael R.; Lobbestael, Sandra J.; Taylor, Charles P.; Hershenson, Fred M.; Miskell, David L., J.Med.Chem., CODEN: JMCMAR, 33(2), <1990>, 854-861; BABS-5500188